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THE RELATIONS OF INTERNAL MEDICINE TO PSYCHIATRY.*

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The subject which I have chosen for my remarks is the relation of internal medicine to psychiatry. Workers in internal medicine who are not psychiatrists will, as a group, look at such a topic from a view-point somewhat different from that of a group of psychiatric workers. Moreover, no two members of either group can be expected to hold identical views, owing to inequalities in innate tendencies and in opportunities for acquiring knowledge. You will not expect me, therefore, with the prejudices of my group and with the bias peculiar to myself, to give expression to opinions wholly satisfactory either to psychiatrists or to other internists. As fellow workers in allied fields of natural science, however, your way of looking and mine are sufficiently alike to permit, I hope, of a similarity of view consistent with sympathy and with conditional approval. It is desirable that from time to time various internists and various psychiatrists shall give expression to their ideas regarding the mutual relations of their respective subjects, for the fruits of such discussion should grow in value with the number sharing in it.

Satisfactorily to deal with my topic, the province of each of the two subjects should be defined; but as with every two sciences which overlap or border on one another, there is likely to be some doubt as to the exact territory of each. As generally understood, *internal medicine* has to deal with the science and art concerned with the restoration and preservation of health by means other than those employed by the surgeon and the obstetrician, while *psychiatry* has to deal with the study and treatment of diseases of the "soul" or "mind," the word "psychiatry" being derived from the Greek ψυχή, meaning breath, life, soul, and ἰατρός, meaning physician. Thus, out of the larger subject, medicine, dealing with all disease other than that dealt with by surgery and by obstetrics, and including diseases affecting both what has been called the mind (ψυχή) and what has been called the body (σῶμα), there has developed a special branch known as psychiatry, in which, according to general assumption, special attention is paid to the diseases which affect particularly the mind.

The actual establishment of psychiatry as a subdivision of internal medicine is of comparatively recent development, scarcely more than a hundred years old. In the medicine of antiquity, it is true, disturbances of the "soul" were thought to be associated with bodily disturbances, especially with fever and with changes in the humors of the body, but this medical view of "mental disease" did not obtain during the middle ages. "Mental disturbances" for the scholars and the priests

* Annual Address at the seventieth annual meeting of the American Medico-Psychological Association, Baltimore, Md., May 26-29, 1914.

of that time were not looked upon as evidences of disease but rather as due to demoniacal possession or divine punishment, occasionally to divine ecstasy or rapture. Medical men up to a century ago busied themselves but little with the study and treatment of those who were grossly disturbed "mentally." The treatment these unfortunates received varied with the disturbance. Some of them were lucky enough to be revered and worshiped as saints, but more of them had the misfortune to be regarded as sinners whose only hope lay in a priest who could exorcise evil spirits; all too often, as witches or wizards, practitioners of sorcery, they were made to feel the tortures of the rack or to suffer at the stake.[1] The interest of medical men had become reawakened in mental disease a long time before it became generally recognized that mental disturbances are best studied and treated by physicians, and it was only after the insane began to be treated in a humane manner in hospitals under the care of physicians that the scientific study of "mental disease" could be begun.[2]

Pinel and Esquirol in France; Reil, Nasse and Jacobi in Germany; Gardner Hill, Tuke and Connelly in Great Britain were the pioneers in ameliorating the conditions by providing medical treatment.[3] In America asylums for the insane began to be established in the first quarter of the last century; the propagandism of Miss Dorothea Dix, in the middle of the century, led to great reforms in care, and with the opening of the Utica State Hospital in 1843 began "the era of awakening."[4] A demand for psychiatric clinics, for the scientific study of "mental diseases," was made by Griesinger in 1868, since when such clinics have been established in Germany in nearly all the university centers. We have begun to follow Germany's example in America; a psychiatric clinic has existed for several years in Ann Arbor; Boston has a psychopathic hospital[5] which serves a similar purpose, and now Baltimore has the Phipps Psychiatric Clinic. During the past twenty-five years psychiatry, in spite of the obstacles in its way, has developed with surprising rapidity, attaining to general recognition as an important medical specialty. The study of patients by clinical methods has led to the recognition of certain types of abnormal behavior, disorders with characteristic symptoms, course and termination. Psychiatrists, calling to their aid the methods, and utilizing the results, of certain of the more fundamental sciences (anatomy, physiology and embryology of the nervous system, normal psychology, pathological anatomy, experimental pathology, pharmacology, general medicine), have been gradually accumulating data for a foundation upon which a true science of psychiatry may later be built, a science which will reveal the nature and causes of what are now called "mental disorders" and which will permit man to cure or to prevent them.

When we inquire why it is that psychiatry has been marked off as a special province of internal medicine, to be cultivated for its own sake by a selected group of men known as psychiatrists, rather than by the general practitioners of internal medicine who deal with diseases of the respiratory, circulatory, digestive, urogenital, nervous and other systems of the body, we find the reasons (1) partly in the historical development above referred to, (2) partly in the fact that, for obvious reasons, the markedly disturbed patients with whom psychiatrists first dealt could not be cared for properly except under conditions differing somewhat form those which obtain in people's homes and in the ordinary wards of hospitals, and (3) partly in recognition that abnormal mental states and the pathological behavior which accompanies them require for their investigation a training and an experience both in normal psychology and in psycho-pathology which have, hitherto, not been available to the ordinary graduates of medical schools.

It was, then, chiefly an urgent practical need, that of caring for patients whose extraordinary behavior was such as to preclude medical attention at home and in ordinary hospitals, which led to the development of psychiatry as a special branch of medicine. It is well that this should be emphasized, for as knowledge of psychiatry and of medicine increases, it becomes ever clearer that there is no fundamental difference between the pathological states studied by the psychiatrist and those studied by the general internist. The patients who ultimately fall into the hands of the psychiatrists are usually observed in the earlier periods of their illness for a longer or shorter time by internists, and many patients who remain in the general internist's care throughout the whole of their illness exhibit behavior which would be recognized at once by those skilled in psychiatry as the accompaniment of abnormal mental states.

Some seem to believe that the domain of abnormal "mental states" is identical with that of psychiatry, belonging exclusively to it, while the domain of abnormal "bodily states" is identical with that of internal medicine, belonging exclusively, in turn, to it. Without entering further at present upon what is meant by "mental states" and "bodily states" respectively, it is obvious that to define the provinces of internal medicine and psychiatry in the way mentioned will be satisfactory neither to the psychiatrist nor to the general internist. For a large part of the work of psychiatrists to-day consists in the study of the "bodily states" of their patients *ante mortem* and *post mortem*, and no small part of the work of internists consists in securing from their patients reports of modifications of their "mental states," known ordinarily as the "symptoms" of which the patients complain.

In the study of every patient, an internist begins with listening to a "complaint." If a patient complain of a pain in the abdomen, of a cough, of a feeling of palpitation, of shortness of breath, of diarrhœa, of dimness of vision, of sleeplessness, of disinclination for exertion, of loss of appetite, of numbness

[1] Kraepelin (E.): Psychiatrie. V. Aufl., Leipz., 1896.

[2] *Cf.* Ziehen (T.): Die Entwicklungsstadien der Psychiatrie. Berl. klin. Wchnschr., 1904, XLI, 777-780.

[3] Garrison (F. H.): An introduction to the history of medicine. Phila. and Lond., 1913; also, Meyer (A.): A few trends in modern psychiatry. Psychol. Bull., 1904, I, 217-240.

[4] Hurd (H. M.): Three-Quarters of a Century of Institutional Care of the Insane in the United States. Am. J. Insan., Jany., 1913.

[5] *Cf.* Southard (E. E.): Contributions from the psychopathic hospital, Boston, Massachusetts: Introductory note. Bost. M. and S. J., 1913, CLXIX, 109-116.

in his left foot, in each instance he reports a modification of his "consciousness" which has led him to assume that his body is diseased, perhaps, in the part of it which feels abnormal to him. This assumption of the patient may or may not be correct; the internist often finds that the patient's "ideas" of the nature and localization of his "bodily disturbance" are erroneous. The physician uses, however, the psychic (anamnestic) clues as guides to his search for pathological-physiological processes; he hunts for physical, chemical, or biological changes, first in the parts to which the patient has referred him, and also elsewhere in the patient's body; very often he gives but little more thought to the "mind" of the patient who has reported one or several modifications of his consciousness. Now there would seem to be easy transitions from these slighter modifications of "consciousness" which we call the "symptoms" or ordinary "somatic" disease, to the outspoken and complex "mental" syndromes with flagrant maladjustment to surroundings with which the psychiatrist has ordinarily to deal. It is the internist's experience with the pain of gall-stone colic, with the delirium of typhoid fever, with the mental confusion of uræmic intoxications, with the hallucinations which accompany enforced abstinence after alcoholic excess, with the depression which accompanies mucous colitis, with the optimism of the consumptive, with the aphasic, apraxic and agnostic phenomena in cerebral atherosclerosis, with the post-paroxysmal homicidal act of a man who has epilepsy, with the delusions of grandeur in general paresis, with the moral and intellectual defects often seen after disease of the brain in infancy, with the dullness, slow-wittedness and drowsiness of myxœdema, and with the anxiety, apprehension, fear, restlessness and irritability characteristic of exopthalmic goitre, which makes him think of the importance of studying "somatic" alterations when the "mind" or "psyche" is disturbed, and of observing the "behavior" of the patient and of inquiring as to changes in his "mental" states when the "body" or "soma" is obviously diseased.

We might further attempt to express the relation which obtains between internal medicine and psychiatry by applying in pathological domains a modern conception of the relation of physiology to psychology,[6] and say that internal medicine (exclusive of psychiatry) investigates the processes (under diseased conditions) of the parts, or organs, of which any organism is composed, while psychiatry investigates the activities (in abnormal states) of the organism as a whole, that is, those activities in which it operates as a whole or unit. But from what has been said of the work now actually carried on by psychiatrists on one side and by general internists on the other, it is plain that these definitions are not entirely satisfactory, though they approach the goal and are doubtless akin to the considerations in which psychiatry is defined as "the science which deals with disorders of adaptation or adjustment of the person to the 'situations' in which he finds himself." If we modify this last definition of psychiatry so as to include only the cases in which there is *conspicuously* abnormal behavior of the person as a whole, we shall come closer to the actual work of the psychiatry of our time. It is not worth while, perhaps, to strive too hard for precision. Even if we could satisfactorily delimit the provinces under discussion to-day, the boundaries would have to be changed a little later on. We must, therefore, forego any attempt at final and rigid mapping, be content with outlining the areas provisionally, and be prepared to change the outlines as the sciences develop, as their methods of study change, or as the needs of practice dictate. Our difficulties would only be increased if we tried sharply to mark out the field of neurology; this doubtless explains why, in some universities, neurology has an independent place, in others is combined with psychiatry, and in still others is kept in the department of internal medicine.

It would certainly not be wise to limit the psychiatrist's studies to what are ordinarily known as the "insanities" or "lunacies," to the patients whose "unsoundness of mind" is, for example, symptomatologically designated as mania, melancholia, dementia, hallucinatory confusion, paranoia, hebephrenia or catatonia, syndromes one or more of which may be met with in the several pathological states known as the manic-depressive psychoses, the idiocies and imbecilities, the toxic and infectious processes, dementia paralytica, the senile dementias, or the psychoses of adolescence (dementia præcox). While the practical side of his work may compel him to give the major part of his time to the study and care of such patients, it is mandatory for the advance of his science that he shall have opportunity to study also (1) some of the patients ordinarily described as "nervous" or "psychoneurotic," rather than "insane," I mean, for instance, the "neurasthenic," the "hysterical," the "psychasthenic," or the "hypochondriacal," and (2) some of the patients, presenting the phenomena known as aphasia, agnosia, and apraxia, due to local lesions in the brain. There is no dearth of such material; every community supplies it in amounts adequate to provide for the investigative needs of the psychiatrists, as well as for those of the general internists and the neurologists. It will be all the better if the psychiatrist can add still further to his objects of study and include a certain number of those individuals who are thought not to be actually diseased but only to be psychologically "unusual," for instance, (1) geniuses, (2) those who have undergone or are reported to have undergone peculiar experiences (hypnotic, mystical, psychotherapeutic, telepathic, etc.), and (3) those who manifest so-called anti-social tendencies (*e. g.*, vagrants, prostitutes, criminals).

Indeed, to build up a general psychopathology, whether it have an associational basis, as in the attempt of Ziehen, or a clinical pathological basis, as in the effort of Wernicke,[7] or be more eclectic, as exemplified by the recent works of Lugaro[8] and of Jaspers,[9] a large and varied clinical and pathological

[6] McDougall (W.): Psychology, N. Y. (Home Univ. Library), 1913.

[7] Wernicke (C.): Grundriss der Psychiatrie. 2 Aufl., Leipz., 1906.

[8] Lugaro (E.): Modern problems in psychiatry, Eng. Transl. by D. Orr and R. G. Rows, Manchester, 1909.

[9] Jaspers (K.): Allgemeine Psychopathologie, Berlin, 1913.

experience is desirable. The general psycho-pathologist can, however, in his constructions, make good use of the results of intensive studies made in more circumscribed fields. He must know how to value in the first place researches dealing with the subjective phenomena of mental disease (phenomenology), whether these are reported by patients as referring to external objects, to persons other than themselves, or to their own bodies, and including not only cognitive states but also feelings and emotions (affective states), and consciousness of effort or striving (conative states). He must understand also how to estimate the objective symptoms of "mental disease," the objectively demonstrable disturbances of perception, comprehension, orientation, association, memory, motility, speech, the bodily expressions of mental states (physiognomy, writing, work, behavior). He will pay attention especially to reports of investigations undertaken from the experimental side.[10] Besides utilizing these studies bearing upon the subjective and objective elements, he has further to determine the worth of researches which deal with the connections which exist among the subjective phenomena, that is, with the way in which systems and dispositions develop in the mind in disease and with the manifestations of the abnormal "structure of the mind" in the so-called "pathological reactions,"[11] in "pathological suggestibility," in "pathological after-effects of earlier experiences," or in the splitting off of smaller or larger systems and dispositions from the mind as a whole ("dissociation of personality"). In this domain come also the observations upon the attitude of the patient toward his own disease, whether it be one of total "perplexity," or one in which he more or less critically observes his own mental state and decides that it is either normal or abnormal (absence or presence of so-called "disease-insight").

The worth of investigations of the connections existing among the elements on the objective side has also to be weighed and judged by the all-round psychopathologist. These connections appeal especially to the worker who has been trained in biology, physics and chemistry, for it is in them that he believes that causal explanations are to be sought. Regarding the structure and functions of a living organism as the resultant of the interactions between factors of heredity and factors of environment, he will enter upon the Herculean task of analyzing, in an individual case, the reciprocal influences of exogenous forces and the innate tendencies derived from the patient's progenitors. Here all the methods of internal medicine—physical, chemical and biological—have to be employed. It is only on a basis of studies such as I have referred to that we can hope in the future for a satisfactory general psychopathology, one adequate for application to the clinical syndromes which we meet every day either as psychiatrists or as general internists. And as our knowledge of general psychopathology grows, our classification of the psychoses and psychoneuroses will gradually change. Clinical syndromes will be multiplied or reduced as further knowledge permits of greater discrimination on the one hand or of better syntheses on the other. Psychological classifications will arise on the subjective side, while on the objective side pathological-histological, chemical, physical, and biological classifications will be established; and, most important of all, we shall ultimately arrive at the groupings which are so important for prevention, namely the etiological.

I have spoken of "consciousness"[12] as though there were no doubt that it occurs. But we live in iconoclastic times, and there are people who deny the existence of "consciousness" as they do that of "ideas" and the possibility of "introspection."[13] Now medical men, as a rule, have had but little training in psychology or in psychophysics. They have had an education in natural science (physics, chemistry and biology), and in the laboratory and clinical branches of medical science. They take it for granted that they are conscious organisms themselves, that other human beings and perhaps animals are conscious, and that consciousness if experienced by lower animals, by plants, or by inanimate objects in the external world must be very unlike their own. They are familiar with different grades of consciousness in themselves from the full awareness of alert states through the lessened awareness of dreams to the "unconsciousness" of deep sleep or of ether-anæsthesia. This consciousness occurs in the same living body which they study in other ways:[14] they do not think of it as anything separable from the living body; it disappears sometimes while the body is alive; they think that human and animal consciousness ceases to exist, as such, at death and often at a considerable period before death when this is preceded by coma.[15] Familiar with the conceptions of development and of adaptation, they think of the gradual evolution of consciousness in each human individual as well as in the animal series; they think of it as having its origin in lower forms of mentality, for they do not think of attributing to the amœba any awareness comparable to their own; since, however, they see a graded series of living organisms extending all the way from the protozoa to man, it is not hard for them to think of similar gradations in the "mental" or "psychic" all the way up to the "mind" of man from the "protoæsthesia" of the amœba. Indeed some medical men, as did Paracelsus and Jerome Cardan centuries ago, can go further and conceive of a "psychic" side to the inorganic world (as in the doctrines of hylozoism and panpsychism).[16] On account of their training in biology and in evolution, physicians think of the mind as developing

[10] *Cf.* Hoch (A.): A review of psychological and physiological experiments done in connection with the study of mental diseases. Psychol. Bull., 1904, I, 241-257.

[11] Meyer (A.): The problems of mental reaction-types, mental causes, and diseases. Psychol. Bull., 1908, V, 245-261.

[12] *Cf.* Marshall (H. R.): Consciousness. N. Y., 1909, 1-685.

[13] See the interesting discussion of this subject by Lovejoy (A. O.), On the existence of ideas. Johns Hopkins Univ. Circ., n. s., 1914, 178-235.

[14] Kraus (F.): Die Abhängigkeitsbeziehungen zwischen Seele und Körper in Fragen der inneren Medizin. Ergebn. d. inn. Med. u. Kinderheilk., Berl., 1908, I, 1-46.

[15] I am, of course, not referring here, in any sense, to the ultimate problem of the "immortality of the soul."

[16] See articles on these subjects in Eisler (R.), Wörterbuch der philosophischen Begriffe. 2 Aufl., Berlin, 1904.

parallel with the increasing complexity of the mechanisms of regulation and association, that is, with the advancing intricacy of the nervous system, in organisms struggling for their own existence and that of their species. They find it natural, therefore, to look upon "consciousness" and upon "infraconscious mind" as in some way indissolubly connected, in human beings and in the higher animals, with the physiological processes going on in the nervous system and the sense organs. They are sympathetic with the doctrine of various levels of reflexes in the nervous system; they recognize that the activities of the lower levels may not be associated with consciousness but think it possible, with Knight Dunlap,[17] that no consciousness occurs without complete arc-reflexes involving the higher levels. In examining the writings of workers in psychology, physicians sometimes find it difficult to understand all that is said in the discussions regarding (1) the difference between "consciousness" and its "content" and (2) the subject-object relationship! Medical men are, however, conscious of "knowing" and "feeling" and "striving" themselves, and they note that these processes occur in cycles which tend naturally to end in feelings of "satisfaction." Observing other people's behavior, they conclude that these others also "know" and "feel" and "strive." They realize that they can be conscious not only of content which is "present" (intuition) but also of content "not present" (imagination). They can recall the past (recollection); learning, too, that what they are conscious of at any given moment has its "meaning" because of earlier experiences, they speak of "memory" and try to explain it by conceiving of some structural modification of the nervous system that endures, labelling the record a "mental disposition" or an "engram." They see that, as minds develop, these "mental dispositions" become exceedingly numerous and are systematically arranged in smaller groups, larger groups and finally in one vast system; on the cognitive side, the total accumulation constitutes, abstractly considered, the "knowledge" possessed by the mind, while on the affective and conative side the total accumulation, abstractly considered, constitutes the "character" of the individual.[18]

Especially interesting to physicians and psychiatrists are the systems of mental dispositions which pertain to the body of the individual in contrast with those which pertain to the "world" external to that body. In all conscious states the background is formed by somatopsychic constituents, that is, by elements referable to the body itself, including the kinæsthetic and visceral sensations, the innervation-feelings, the appetites, and the aversions, and the various so-called affective or emotional states. Our bodies are always "with us"; they are being continually experienced in our conscious states; the "content" corresponding to these bodies is relatively constant as compared with the infinite variation of the "content" corresponding to the external world. No wonder that this "content" pertaining to the body seems to be peculiarly our own; it is "private" content in contrast with that content which (in a sense, but only in a sense) can be publicly shared. No wonder that we speak therefore of the "self," and define introspection in the narrower sense as "observation of the self," remembering, however, that in the wider sense introspection may refer to examination of the total content. Nor is it surprising that many find it desirable to designate the "observer" as the "I" or "Ego," the "subjective correlator of experience" in contrast with "what is observed," *i. e.*, with the content ("self" and "not self").[19] In this connection it is well to keep in mind the fact that the body is an agglomerate of organs and that the conditions dealt with by the physician often involve gross alterations in the elements of this organ-agglomerate. It is surely not surprising, that somatic disease is often accompanied by alterations in the "self" which have a peculiar tendency to persist and to be characterized by negative feeling tones.

Medical men are not likely to give up the study of consciousness or to refuse to use the reports given by patients of their "subjective" experiences.[20] Such a policy would seem to them absurd. But wedded as they are to the method of investigation of the natural sciences, they welcome objective methods of study whenever these are feasible. This predilection, together with the naturalist's tendency to resort when possible to comparative[21] and genetic methods, accounts for the physicians' sympathy with the "behavior psychology" of our time. The study of animal behavior by men like Loeb[22] and Jennings[23] has given us entirely new conceptions of instinct and of intelligence, of the nature of so-called "purposive activities," of the bases of human nature, and of the evolution of mind in the animal series up to man. Recently a number of psychologists —the so-called behaviorists—have tried to eliminate introspective methods in psychology and to describe the whole mental life of man in terms of "expression" or "behavior." Starting with the conception of the neuropsychic reflexes (inherited nervous mechanisms modified by past individual experience) they study the responses to external stimuli (reflex responses) and to internal stimuli (automatic responses) as manifest in movements, vasomotor activity, or gland secretion. In this country, Watson[24] and Meyer[25] are well-known advocates of behavioristic studies. Recently the Russian neurologist, v. Bechterew,[26] in a book entitled "Objective Psy-

[17] Dunlap (K.): A system of psychology, N. Y., 1912; also, Images and ideas. J. H. Univ. Circ., 1914, 161-177.

[18] *Cf.* McDougall (W.): *loc. cit.*

[19] *Cf.* Dunlap (K.): *loc. cit.*

[20] *Cf.* Angell (J. R.): Psychol. Rev., 1913, XX, 255-270.

[21] *Cf.* Herrick (C. J.): Some reflections on the origin and significance of the cerebral cortex. J. Animal Behavior, 1913, III, 236.

[22] Loeb (J.): Comparative physiology of the brain and comparative psychology, N. Y., 1900, 1-309; also, The mechanistic conception of life, Chicago, 1912, 1-232.

[23] Jennings (H.): Behavior of the lower organisms. N. Y., 1906, Macmillan Co., 380 pp., 8°.

[24] Watson (J. B.): Psychology as the behaviorist views it. Psychol. Rev., 1913, XX, 158-177; also, Image and affection in behavior. J. Phil., Psychol., etc., 1913, X, 421-428.

[25] Meyer (M.): Fundamental laws of human behavior. 1911.

[26] v. Bechterew (W.): Objective Psychologie. Leipz. and Berl., 1913, 1-468. See Review by H. C. Warren in Science, N. Y., 1914, n. s., XXXIX, 426-428.

chology" has made a consistent and fairly successful attempt to view human psychology from this standpoint. The "conditional reflexes" (involving associative memory) can be studied in several ways. Pawlow taught us the use of the "salivary method" in the dog; Weber, in Kraus's clinic in Berlin, worked with the vasomotor method; Bechterew uses a special method, that of motor association reflexes. In studying the more specialized forms of complex responses, Bechterew describes the "concentration-reflex" (the behavior analogue of attention), the "symbolic reflex" (analogue of language), and the "personal reflex." As a program of study likely to be fruitful, behavior psychology would seem to be highly commendable; but in its more dogmatic statements, its denial of the value of introspective methods, its total repudiation of "images," medical men are not likely wholly to concur.

Internal medicine and psychiatry, confronted as they both are by the problems of the physical and the mental,[17] must obviously be directly and deeply concerned with the nature and origin of knowledge (epistemology) and with the nature of reality (ontology). Starting out, as every one must, with naive notions regarding the world of things we know and as to how we know it, physicians come gradually and more or less unconsciously to the adoption of certain epistemological and ontological theories. Though there is no unanimity in opinion among medical men, their special training and experience make them much more sympathetic with some tendencies than with others. First of all, they desire to stick close to experience, lauding the empirical and deprecating the speculative; but, despite this tendency, which on the whole is a good one, they often refuse to theorize when it would be helpful, and they are ever unconsciously transcending experience. In the second place, brought up in the school of the natural sciences, saturated with mechanistic explanations, the medical mind has a structure which predisposes it, at least at the beginning of its critical and philosophic interests, to what metaphysicists designate as materialism and realism, rather than to what they call idealism.

On talking with a number of the more reflective among the medical men I know, and on reading opinions in the literature, it would seem that the critical medical mind of to-day is appealed to especially by the natural-science theory of knowledge[18] (W. K. Clifford, Karl Pearson, E. Mach, W. Ostwald, H. Poincaré), but as regards theories of being it is less uniformly responsive. Many physicians lean toward a phenomenal idealism which is not far removed from realism (*e. g.*, Immanent Philosophy of W. Schuppe; Empirio-criticism of Avenarius; Energetics of W. Ostwald and Lasswitz); others adopt a personal idealism (*e. g.*, Humanism of Schiller; Pragmatism of W. James, J. Dewey, and H. Bergson); still others are captivated by some form of realism (*e. g.*, Intuitive Realism of the Scotch School; Synthetic Philosophy of H. Spencer; the New Realism of Woodbridge, Montague, Holt and S. Alexander). Occasionally a physician adopts an out and out idealism (*e. g.*, Neo-Hegelian Rationalism or Absolutism of B. Bosanquet; of J. Royce), and, here and there, one, reflecting upon the issues between the realists and the idealists, accepts a kind of synthesis of pragmatism and rationalism, trying to avoid the extremes of each (*e. g.*, Theism of J. Ward; of E. H. Griffin[19]). A large number of medical men decline to let their pia mater be stretched by metaphysical considerations at all; many assume either an agnostic attitude, or at least one of suspended judgment.[20] Psychiatry, then, as I see it, is a large and very important chapter of Inner Medicine. Every internist should have at least some training in psychiatry, and every psychiatrist should be well-versed in the fundamental facts and methods of study of general medicine. Psychology—both introspective and behavioristic—is just as important as a preliminary study for the prospective medical student as physics, chemistry and biology.

Considering the disadvantages under which psychiatry has worked in the past, the science is certainly to be congratulated upon the fine minds it has attracted and upon the results it has accomplished under difficulties. Full of fascinating problems, psychiatry is in the near future, I venture to aver, likely to prove a formidable rival of all the other medical specialties for the affections of the better young men now entering upon medical careers. We have only to think of the very important social relations of psychiatry to understand that this must be so.

Contemporary psychiatry shows no timidity in the tasks it is assigning itself.[21] On the contrary, it manifests an ardor and a courage typical of youth. It does not limit itself to the mere study of the insane or the manifestations of insanity. It desires to investigate the cerebral events underlying the abnormal mental states. It is not satisfied with normal psychology or with brain-anatomy and brain-physiology as they exist to-day, and insists, that at least some psychiatrists make contributions in these fields. It studies the pathological anatomy and histology of the brains of the mentally diseased, but it does not stop at the local changes in the brain; it studies also the changes in other organs of the body, seeking abnormal processes there which can account for abnormal brain processes. Then it tries to discover in a faulty heredity, or in environmental influences, explanations of these abnormal processes. Psychiatry studies also the evolution of mind in the individual and in the animal series, and tries to relate this evolution to studies in comparative anatomy and physiology. It does not try to escape from the borderlands of philosophy and metaphysics, but actually ventures into these neighboring territories, taking part, as we have seen, in attempts to construct a theory of knowledge and theories as to the nature of reality.

[17] *Cf.* Warren (H. C.): The mental and the physical. Psychol. Rev., 1914, XXI, 79-100.

[18] For a good epitome of such views, see Kleinpeter (H.): Die Erkenntnistheorie der Naturforschung der Gegenwart. Leipz., 1905, 1-156.

[19] *Cf.* Griffin (E. H.): Some present-day problems of philosophy. Johns Hopkins Univ. Circ., 1914, 140-160.

[20] For welcome summaries of current philosophical views, see (1) Perry: Present philosophical tendencies . . . . , and, Caldwell (W.): Pragmatism and idealism. Lond., 1913, 1-265.

[21] *Cf.* Lugaro (E.): *loc. cit.*

Psychiatry has, surely, no narrow conception of its plan of work.[33] The technical knowledge demanded for a successful attack upon all its problems is enormous. The methods of a whole series of subsidiary sciences must be drawn upon. No single investigator, of course, can hope to be active in all parts of this large and varied field of inquiry. Not even the collective activities of the members of a single psychiatric clinic can cultivate more than a small portion of the field. The work is cut out for the aggregate of the world's psychiatrists for at least many generations ahead.

The general internist can, perhaps, do most to help psychiatry progress by studying carefully the bodily "equivalents" of psychic phenomena, the contractions of striped and unstriped muscles, the activities of the glands of external and internal secretion, the respiratory and vasomotor changes, and the modifications of cœnæsthesia. Present-day studies of the abnormalities of the functions of the autonomic nervous system[34] on the one hand, and of the diseases of the ductless glands (endocrinopathies)[35] on the other, and their relations to the mind, are instances which illustrate the possible influence of Inner Medicine on a developing Psychiatry. We have far to go, but we are on the way.

[33] *Cf.* Meyer (A.): A short sketch of the problems of psychiatry. Am. J. Insan., 1897, LIII, 538-549.

[34] *Cf.* Barker (L. F.) and Sladen (F. J.): The clinical analysis of some disturbances of the autonomic nervous system, etc. Trans. Asso. Am. Phys., 1912, XXVII, 471-502; also, Barker (L. F.), the clinical significance of the autonomic nerves supplying the viscera, and their relations to the glands of internal secretion. Can. Med. Asso. J., Montreal, Aug., 1913.

[35] Biedl (A.): Innere Sekretion. II Aufl., Wien, 1913.

KORSAKOW'S PSYCHOSIS OCCURRING DURING PREGNANCY.*

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During gestation or the puerperium various forms of paralysis may occur, which may be either of (1) central or (2) peripheral origin. For instance, many cases of hemiplegia have been described which have developed during childbirth either as a result of a hæmorrhage, embolus, or thrombus, and it is by no means rare to meet with cases of paralysis of the peripheral nerves either of traumatic (*e. g.*, from pressure on the nerves as they pass through the pelvis), or of toxic origin. It is this last form—the so-called toxic form—to which I want to direct attention. The earliest reference to this subject which I have been able to find is an article written in 1854 by Fleetwood Churchill "On Paralysis Occurring During Gestation and in Childbirth." In this article Scanzoni of Wurzburg is quoted as having said that paralysis of the lower extremities may in some cases be due to pressure, but in other cases, as the paralysis did not appear until some time after labor, and as a similar affection is known to have attacked the upper extremities, pressure could not be the sole cause, *and it may be attributed to some more profound derangement.* Furthermore, Churchill described as occurring with pregnancy a series of 35 cases of various forms of paralysis, 22 of which occurred during pregnancy, and 13 either during or a short time following delivery. Unfortunately the case records are exceedingly brief, and the cases in the light of our present-day knowledge are so indefinite and heterogeneous that it becomes difficult to estimate even approximately how many of these cases were really cases of peripheral neuritis due to an unknown toxin, how many were of central origin, and how many were of psychogenic origin. To my mind there is no doubt but that some of these were cases of polyneuritis, due to the process of gestation, but owing to the somewhat imperfect description one would hesitate to make use of them. In 1867, however, Boulton described the case of a multipara, 38 years, who during the eighth month of her pregnancy lost the use of her limbs; could not stand; could not grasp anything, but was able to move her extremities fairly well. Her sensibility was also much diminished. Later her knees became contracted, and pain was experienced in extending them. She was constipated, her appetite was poor, and she fell off in weight. In regard to her mental condition, it is stated that she answered questions rationally, *but her memory was entirely gone.*

Two months after coming under observation she was delivered of an eighth month child in a state of decomposition. The patient made a good recovery from her confinement, but did not improve in memory, for in less than one week she had quite forgotten that she had ever been confined. The above case is no doubt one of polyneuritis, occurring during pregnancy, but except for a few other isolated case records the subject appears to have received scant attention until Möbius, in 1887, put together a series of seven cases of peripheral neuritis, affecting principally the median and ulnar nerves. Möbius' cases all showed themselves during the puerperium, but he advanced the hypothesis that they were probably due to some form of poison formed during gestation. In addition to those forms of neuritis localized to one limb, Möbius in a further communication in 1890 described a generalized form in a woman 30 years old, who four weeks after confinement complained of pain in the left hand, and pricking and burning sensations in both hands. Later the strength of her arms and legs became considerably diminished; all the muscles were flaccid, and wasting occurred in the hand muscles. Möbius makes no special mention of the mental condition in any of his patients. It is not until the appearance, in 1887, of Korsakow's classical de-

* Read in abstract before the American Medico-Psychological Association, May 28, 1914.

scription of the polyneuritic syndrome that we begin to have a more thorough understanding of the disease.

Korsakow grouped together a number of cases of apparent toxic origin, associated with polyneuritis, which were characterized by poor power of retention for recent events, disorientation for time and place, misidentifications, and confabulations, *e. g.*, the description of fictitious journeys and episodes. It was found that this psychosis developed most frequently on the basis of chronic alcoholism, but that it also occurred in connection with other toxic, and infective agents, *e. g.*, in febrile states, lead poisoning, and pregnancy. *Later investigation also showed that the polyneuritic symptoms need not be a constant accompaniment of the psychosis.*

Korsakow reported the case of a woman, 28 years, who towards the end of gestation had œdema of the legs, as well as pain in the limbs, and in the neighborhood of both sciatic nerves. On October 3, 1880, a dead, decomposed child was born. On the next day the patient was in an excited, confused, fearful state. Later she developed anæsthesias and paræsthesias of her extremities, the muscles of the lower limbs were paralyzed, and then the extensor and interossei muscles of the arms and hands became affected, and finally the back and abdominal muscles. Pain was present in the back, in the arms, and in the region of the fifth nerve. Choreic and athetoid movements developed in the legs and arms, and there were also present twitching of the face muscles, swallowing difficulty, and a transitory speech disturbance. It was exceedingly difficult for the patient to concentrate her attention, her memory was poor for recent events, particularly for time, so that she could not tell whether an event had happened the day previously or three years previously. She asked the same question over and over again. After a period of ten months a marked improvement had taken place in the patient's condition. After a period of four years the patellar reflexes returned.

Owing to the fact that cases of Korsakow's psychosis occurring during gestation are exceedingly rare, I have felt that it would be of considerable interest to report two further cases, one of which was associated with a tremendously generalized polyneuritis, while the other showed no polyneuritic symptoms, but mentally the picture was characteristic.

Case 1.—A young married woman, 31 years, was admitted to the Henry Phipps Psychiatric Clinic on September 4, 1913. She had come of a healthy stock, and had developed normally. She married in April, 1906, and in April, 1907, her first child was born. During this first pregnancy she suffered from nausea and vomiting for three or four months, but did not show any nervous manifestations. The delivery was instrumental, but the puerperium was normal, and she nursed the child for nearly one year. Up until the onset of the present trouble she had been in her normal good health. Early in May, 1913, the patient became pregnant for the second time; towards the end of the same month her appetite became poor, and she started to suffer from nausea. During the months of June and July she was vomiting almost constantly, and lost from 30 to 40 lbs. in weight. She became terribly weak, could only walk with assistance, and it was noticed that her feet would flop. In July, 1913, numbness in feet, legs, and hands developed, but up until about August 6, 1913, she was able to take a step or two. No mental disorder of any kind was noticed until about August 2, 1913, when one morning she suddenly made a number of entirely false statements, *e. g.*, that she had had three glasses of milk (when she had only had one), that a certain young lady had been to see her, that her sister had brought a red-haired girl into the room, that her brother (dead for four years) was downstairs, and when asked to go to town said that she had been there already that morning and was too tired to go again. She became depressed and tearful, thought that her husband was sick, and would cry in a hysterical way on seeing him. She did not seem to have any realization of where she was, kept absolutely no track of time, and when her birthday came around on August 4, denied that it was her birthday. On account of the fact that the patient, both mentally and physically, was getting rapidly weaker it was determined, on August 9, to produce an abortion, the patient now being three months pregnant. A slight laceration of the cervix resulted, her temperature became very slightly elevated, but the blood and urine examinations were negative, except for a somewhat diminished urea output, which a few days later became normal. Almost immediately after the abortion she became delirious, was fearful, thought that she was on a ship, that the ship was sinking, that some one was after her father to kill him, that the house was on fire, and that the fire was coming into her room. She then seemed to lose her voice, could only talk in a whisper, and had great difficulty in breathing. About ten days after the abortion had been performed she lost power in her hands completely, had incontinence of urine and fæces, and became very dull. The patient had never at any time been addicted to the use of alcohol, and there was no known source of infection to account for her sickness.

On admission (September 4, 1913), the patient was delirious, and showed a very unstable emotional condition, laughing one minute and crying the next. She seemed frightened, talked constantly of having been bitten by a dog, but could not tell when, and frequently answered questions in an irrelevant way. She thought that the dog was in the room with her (visual hallucination), and said that she wanted to go and see the doctor about the dog-bite. She misidentified the physician and the nurse, and stated (erroneously) that another gentleman present was the physician's brother. She was completely disoriented for time and place, said that the month was February (September), could not tell the day or the year, and thought that she was still in her home town. She had no realization of her condition, denied that she had any trouble in any way, but admitted that her head felt dizzy.

Physically.—She was in a weak, exhausted, poorly nourished condition, and showed the characteristic symptoms of a generalized polyneuritis; *e. g.*, her hands were flexed at the wrists, extended at the metacarpal-phalangeal joints and flexed at the phalangeal joints (double *main-en-griffe*). She had a symmetrical atrophy of the small muscles of the hands on both sides, and except for occasional slight separation movements, could not move the fingers. The muscles of the forearms were also symmetrically atrophied and flabby, and she could not extend her wrists or carry out pronation and supination movements of the forearms. The muscles of the upper arms were fairly well preserved, so that she could raise her arms above her head. Her feet were kept extended in the position of talipes-equinus, and she was quite unable to move either her toes or her ankles. The muscles of the calves were atrophied and flabby, but at the knee and hip joints she could carry out weak flexion and extension movements, and could abduct and adduct the legs. She could not grip at all with either hand, and could not stand or walk. Her sensory functions were exceedingly difficult to accurately test, owing to her ready exhaustion, and to her confused mental condition. A rough examination showed that to touch sensa-

tions over the hands and forearms on both sides there was a sluggish response, and at times she failed to reply at all when touched on the hands or fingers. She failed to respond to pin-pricks over the hands and fingers, and could not differentiate between the head and point of the pin. This anæsthesia and analgesia gradually lessened up to the elbow on either side; above the elbow the sensibility to touch and pin-pricks seemed about normal. Thermal sensations were more or less accurately differentiated all over.

In the legs and feet the sensory disturbances were analogous to those obtained in the upper limbs; there was an anæsthesia and analgesia extending and gradually decreasing up to the knee-joint. Above the knee there did not seem to be any definite sensory disorder. Marked tenderness was elicited on deep pressure of the muscles of the legs and arms. The tendon and superficial reflexes were completely abolished on the two sides; there was involuntary micturition and defæcation.

With faradic stimulation so much pain was elicited that the examination could not be thoroughly carried out. To galvanism the dorsal interosseous muscles of the feet gave a typical reaction of degeneration, the anodal closing contraction being greater than the cathodal closing contraction; otherwise over the hands and forearms, and legs, the response to galvanism was sluggish, required a large current and the anodal closing contraction approximated the cathodal closing contraction.

In addition to the above, she had a double adductor paralysis of her vocal cords (Dr. Slack), in consequence of which she could not speak above a whisper. She showed a well-marked tachycardia, her pulse rate varying from 130 to 140 per minute, and being irregular in rhythm. Her breathing was entirely costal, owing to the fact that her diaphragm seemed completely paralyzed, and during inspiration the abdomen instead of being protruded was retracted; her breath rate varied from 32 to 40 per minute. There was no disease of the internal organs, and no difficulty in swallowing. Her temperature was 99.8°. A pelvic examination by Dr. Guy L. Hunner, blood examinations, and cultures from the throat were entirely negative. There was a trace of albumen in the urine.

Following Admission.—For several days the patient continued to show a very unstable, emotional condition; at one time she would be bright and laughing, and then again restless and tearful. At nights especially she would get fearful, would think that she was going to be killed, and talked a great deal about people dying. She suffered from visual hallucinations, insisted that people were hiding behind her bed, that some one was trying to kill her child, that bed-bugs, which she attempted to kill, were crawling over her. She remained completely disoriented for time and place.

On September 12, 1913, she was noted as much stronger; her temperature was 99.5°, her breathing was still entirely costal in type, varying in rate from 28 to 32 per minute, her pulse rate was still from 130 to 140 per minute, but was of much better force and volume than previously. She stated that she felt much less fearful than formerly, and only suffered from occasional visual hallucinations at night, Her head felt confused, she continued to misidentify those around her, and confabulated, saying that yesterday she had been up, had gone out driving, and paid a visit. She was still completely disoriented for time and place. Her power of retention was found to be exceedingly poor, as after two minutes she had entirely forgotten an address, the name of a city, and a color, which she had been asked to remember; even after three readings she was quite unable to give the gist of any short story read to her.

On the morning of September 18, 1913, it was noticed that the patient was in a semi-stuporous state, and during the day had a spell of tremendous excitement, waved her arms about, had an agonized expression, and complained of a sensation of smothering. Her pulse became weak and irregular, so that it could hardly be counted, her breathing was quick, intense, about 36 per minute, and her temperature rose to 102 degrees. For three days her condition was exceedingly critical, and she had to be frequently stimulated with strychnine, digitalis and camphorated oil. She finally made a remarkable recovery, and on October 1, 1913, she was able to speak more clearly, but her voice was still husky. She now seemed to have a better realization of things in general, but she still continued to be confused, was exceedingly emotional, and still remained disoriented for time and place. During October she showed a gradual and marked improvement both mentally and physically. She now did not confabulate at all, did not suffer from any hallucinations, and became oriented for place. She continued, however, to be very emotional, laughed and cried in an impulsive way, and was quite unable to keep track of time. Perhaps the most striking thing in her condition now was the marked defect in her power of retention; she would ask the same questions over and over again and in a few minutes after being visited by her friends had no recollection of their visits.

Physically, her voice was now quite natural, but in speaking she would hesitate and stutter over difficult words; her respiration was still costal in type, but was slower and easier, and now varied in rate from 24 to 28 per minute; her pulse continued to be on an average 130 per minute, but her temperature was quite normal. She regained control over her bladder and bowels. Her arms and legs became much less tender, and she became able to carry out slight movements in the fingers, wrists and ankles. Menstruation restarted, and has been quite regular ever since. Since November, 1913, the patient has gone on steadily improving in every way. At the present time (April, 1914) she is bright and interested in everything that goes on around her. Her general behavior is that of a normal person, but as tested by word-pairs, short stories, repetition of numerals, and so on, her power of retention is still poor, but has considerably improved. Her memory for remote events is excellent. Emotionally, she is rather unstable, but gradually is getting better and better control of herself. Physically, she is able to take part in the occupation classes, can embroider, and can attend to herself generally. She can take a few steps without assistance, and can walk from 20 to 30 yards with assistance. Her cutaneous sensory disorders are improving, there is no tenderness elicited on deep pressure of the muscles, but the tendon reflexes cannot be elicited. Her pulse rate varies from 90 to 108 per minute, and her breathing is now thoracico-abdominal in type. Arrangements have been made for the patient to leave the hospital in a few weeks.

The case may then be briefly summarized as follows:

A multipara, 31 years, in the first month of her second pregnancy started to suffer from nausea and vomiting, and rapidly lost in weight. She then complained of numbness and weakness in the feet, legs, and hands. She became depressed, started to fabricate, lost track of time, and was getting worse so rapidly that an abortion was performed when the patient was three months pregnant. A delirium with fear reaction ensued, she lost power in her hands completely, had incontinence of urine and fæces, aphonia, paralysis of the diaphragm, and, probably, also at this time, tachycardia.

On admission to the hospital the patient was delirious, and showed the characteristic symptoms of a generalized polyneuritis. In addition, she had a double adductor paralysis of the vocal cords, and involvement of both the phrenic and vagus nerves. During her hospital residence the striking points in her mental condition have been the exceedingly poor power of retention, the tendency to confabulate, and the un-

stable emotional condition. Both mentally and physically a wonderful improvement has resulted.

The second case which I wish to report is, also, exceedingly interesting, and differs from the first in that the psychosis was not accompanied by any polyneuritic symptoms.

Case 2.—F. I., 37 years old, was admitted to the Henry Phipps Psychiatric Clinic on December 21, 1913.

Family History.—Paternal grandfather was excitable, and her paternal grandmother had hysterical spells. Her maternal grandfather was eccentric. Her father, one brother and two sisters were described as nervous.

Personal History.—The patient was the youngest of a family of seven. She is stated to have been a healthy child, and to have developed normally. She was clever at school, and was interested in everything. She was very even-tempered, was not extreme about anything, and was devoted to her family and home. In 1896 she married, when 20 years old; her married life was exceedingly happy. Except for an attack of typhoid fever one year after marriage she had been perfectly well up until the onset of the present sickness. She had never taken any alcohol, and no history could be obtained of any toxic or infective agent. She had had three previous pregnancies, each of which had been accompanied for two months by vomiting, but in none of these pregnancies were any nervous or mental symptoms noticed.

Onset of Present Sickness.—The patient became pregnant for the fourth time about August, 1912. During the second month of her pregnancy she started to suffer from uncontrollable vomiting, which continued during her entire pregnancy. On account of her vomiting she was nourished during the last five months of her pregnancy principally by nutrient enemata, and altogether lost from 60 to 70 pounds in weight. Her labor was easy, and a full term healthy child was born on March 24, 1913. For two months previous to the birth of her child her husband had noticed that she could not remember things that happened from day to day, but remote events were accurately retained. She described herself as confused, complained of a feeling of pressure and weight in her head, but knew every one around her and was clear in regard to her surroundings. She became apathetic and uninterested, and after the birth of the child hardly seemed to realize that she had had one. About two months after the birth of the child she accused her husband of infidelity; stated that something had been put into a glass of water to affect her, and later that her mind was full of all kinds of profane thoughts. She tended to fabricate, said that a physician had told her certain things in regard to her sickness, and that three ladies had told her that they had suffered just exactly as she had. (All of which statements were false.) On her journey to the hospital she told about being able to see Christ, and told about carrying on conversations within her head with Him. There was no history of any polyneuritic symptoms.

On admission, the patient was apathetic and listless, but talked freely, and answered all questions quite promptly and relevantly. She complained of a spinning sensation, and a feeling of pressure in her head, which seemed in some way to affect the nerves of her eyes; she said that she could not read; could not develop any interest in anything, and felt as if she was a stranger to her self. She described many other curious sensations and feelings, *e. g.*, that her brain consisted of two parts, one normal and one abnormal, that there were obstructions in the blood-vessels of her brain. One of the most peculiar of her symptoms was a pseudo-hallucinatory state in which she saw the figure of Christ, and at other times had visions of beautiful forests, knights, and gay people. In reference to these things she would say: "It is all a figment of the brain I suppose, but it is just as real as my being here talking to you now." In addition to the visions, from time to time she would seem to hear a voice telling her to "be comforted," and that also she clearly recognized as being "purely a mental thing—a thought." At first she was correctly oriented for time and place, but it was very striking to notice how poor her memory was for the names of persons, and her total inability to give an idea of the onset and course of her sickness, and of events immediately preceding admission. The later period of her gestation was apparently almost a blank to her. She did remember that her baby had been born towards the end of March, 1913, but absolutely denied that there had been anything wrong with her in any way until six weeks after its birth. She had no idea, for instance, that for several months she had been nourished almost entirely by rectal enemata; she could not tell when she had come to Baltimore (three days previous to her admission); could not tell what hotel she had stayed in, and did not remember her examination by a neurologist. She had entirely forgotten a name, address, and color, after four minutes. Her memory for remote events, and her grasp on matters of general intelligence were well retained. She had a very good realization of and insight into her condition, frankly admitting that her memory for recent events was poor, and that her pseudo-hallucinatory state was due to her imagination and general nervousness.

Physically, the patient was a well-nourished woman, who showed no disease of the internal organs. Her sense of smell was defective on both sides, as she could not recognize cloves, peppermint, or whiskey. Otherwise, there were no neurological signs. Her pulse, temperature, and respiration rate were normal.

Following Admission.—During the whole period of the patient's hospital residence she continued to present almost the same picture as on admission. She had to have some one constantly with her trying to encourage, stimulate and employ her in every way, but despite the utmost help she would constantly complain of peculiar spells, in which she would close her eyes tightly and show facial grimacing. In these spells she would complain of something of the nature of an iron weight pressing against her brain, and would lose all use of herself. She suffered from sensations as if she were falling from a great height, and her pseudo-hallucinatory state remained constant.

The feature, however, which was of most interest in the case was her exceedingly poor memory for recent events, and her defective power of retention. Her retention was tested by means of giving her three different things to remember, by short stories, by word-pairs, and repetition of numerals; with all of these gross defects were easily elicited. In addition to these defects, a good idea of her state of mental confusion may be gotten from the following facts: One morning she put on her dress before her undergarments; another time she put two dresses on; she was occasionally unable to find her own room on the ward; she would not infrequently after a bath start to put her clothes on without drying herself. She, also, during her hospital residence, became disoriented for time, could never tell the day, date, or month, and was uncertain as to whether the year was 1913 or 1914. An attempt was made to benefit the patient's condition by means of thyroid extract medication, but no benefit resulted. The patient was discharged on April 12, 1914, in an unimproved condition.

In this case, then, we have a woman 37 years old, who up until the onset of her present sickness seems to have been healthy and normal in every way. In all three previous pregnancies we have a history of vomiting of short duration. During her last (fourth) pregnancy, however, uncontrollable vomiting apparently played such a role that the patient became emaciated, and during the last two months of gestation developed a psychosis characterized by apathy, forgetfulness, suspiciousness, and then later by a peculiar pseudo-hallucinatory

state, and a tendency to fabricate. During her hospital residence her mental confusion, her exceedingly poor power of retention, her disorientation for time, and her pseudo-hallucinatory state were the outstanding features.

How are we to interpret such a condition? From the point of view of symptomatology many of the symptoms might tend to make one think that here we are dealing with a case of dementia præcox, and that the pregnancy was merely incidental. In support of such a view the apathy and listlessness, the peculiar ideas, such as one part of her brain being normal and the other abnormal, and the pseudo-hallucinatory state would be advanced. After all, however, the point which impresses one most is her extraordinary defect in memory and in power of retention, and that associated with good insight into her condition is so foreign to the types of dementia præcox that we know as alone to be almost sufficient to rule out such a diagnosis. The explanation that I feel justified in putting forward is that here we have an individual who, on account of the uncontrollable vomiting of pregnancy, became so emaciated and exhausted that definite organic changes resulted, in consequence of which a specialized portion of her memory became deeply affected. With such a lowering of the general level, it seems to me quite understandable why the psychogenic material which no doubt has been dormant in the patient should be expressed. This case, as far as a fairly thorough review of the literature has taken me, seems to be unique, but is in harmony with Korsakow's original observation that *"polyneuritic symptoms need not be a constant accompaniment of the psychosis."*

Furthermore, this case corresponds to those of the toxic-infectious group which Hoch has designated by the term Amentia. In connection with his cases Hoch has emphasized the fact that Freudian mechanisms undoubtedly play an important role, but do not alter the main facts of the clinical picture.

Before attempting to draw any general deductions from these two cases, it would seem well to consider some of the cases described by others, so as to see whether we can get at any factors which are more or less constantly present. I want especially to direct attention to those cases which have shown a Korsakow's symptom-complex, and to those with a generalized neuritis, but without any mental symptoms. I have already made mention of Boulton's case, and of the cases described by Churchill, Möbius, and Korsakow.

Madge in 1871 reported the case of a multipara, 36 years, who at the fourth month of her third pregnancy started to suffer from severe pains in her hands and feet, which became exceedingly sensitive and painful. Later the patient developed an anæsthesia and complete paralysis of her hands and feet. In this case the patient's mind is stated to have been confused, and her memory was impaired. Under electrical treatment improvement occurred in her general condition. It is very interesting to note that about one year after her illness had started the patient was delivered of a dead fœtus of about four months, which to all appearance had been retained in the uterus for many months.

Whitfield's case.—A multipara, 40 years old, on August 7, 1888 gave birth at full term to her seventh child. From the beginning of her pregnancy the patient had suffered from uncontrollable vomiting, on account of which she lost about 80 pounds in weight. Two weeks previous to her confinement her legs felt cold, she partially lost the use of them, and had to be assisted up and down stairs. The day after labor vomiting ceased, but she soon started to complain of pain and "pins and needles" in her legs, and thirteen days later had almost lost the entire use of her arms and legs. Pain was easily elicited on deep pressure over the nerve trunks. The knee-jerks and other tendon reflexes were absent.

The case described by Desnos, Joffroy, and Pinard, again emphasizes the important part played by uncontrollable vomiting in the development of such states.

A multipara, 41 years, had had two previous pregnancies, and was in an anæmic condition. During her third pregnancy the uncontrollable vomiting was alarming, and at the end of the fourth month the lower limbs were markedly atrophied, and this was followed two or three days later by an atrophy of the arm muscles. There was no reaction of degeneration, no disorder of sensibility, and no loss of sphincter control. There was a marked diminution of the patient's intellectual power, especially of her memory. Artificial abortion was performed, and was almost immediately followed by a betterment of the patient's condition. Function finally returned to the muscles and the patient was cured.

Polk, under the title "Mania and Multiple Neuritis in Pregnancy," described a case which terminated fatally at the fifth month. The term "mania" is apparently used by Polk as synonymous with "excitement," because there is nothing at all in the description of the case to make us think of a manic-depressive excitement. On the other hand, the mental condition as described by Polk seems to have consisted essentially of a delirium with fear reaction, and a poor memory for recent events. The case indeed is very similar to the first one reported by me in this paper.

A multipara, 28 years, during the second month of her second pregnancy started to suffer from nausea and vomiting, on account of which she became markedly emaciated. At the fourth month of gestation the vomiting ceased. At this time the patient became delirious and excited, talked in an incoherent way, and seemed to have no realization of her condition or surroundings. She thought that there were gloves on her hands, and asked to have them pulled off, and expressed many rapidly shifting "delusions." She soon forgot every statement made to her. Associated with this mental condition, there was paralysis of both the flexor and extensor muscles of the hands, entire loss of grip, atrophy of the forearms, paralysis of the muscles of both legs with foot-drop, some movement in the thighs, but none in the toes or feet. She complained of various paræsthesias and tenderness was easily elicited on pressure of the muscles. There was involuntary micturition. The respiratory muscles next became affected, and death resulted at the fifth month.

In Handford's three cases the paralysis came on immediately

after confinement; the third one should probably be ruled out altogether, as not belonging to this class of cases. In none of the three cases have we any mention of the mental condition of the patient.

Case 1.—Multipara, 43 years, three days after confinement lost the power in her legs completely, had the sensation of "pins and needles" in the arms, a short time later paralysis of the arms. The muscular sense became impaired, there was impaired cutaneous sensibility, and greatly increased deep sensibility; knee-jerks were absent, the reaction of degeneration was present in both arms and legs. In twelve months the patient was comparatively well.

Case 2.—Woman, 34 years, had complete paralysis of extensors of toes and flexors of ankles, with weakness of most of the other muscles of the legs coming on immediately after confinement. There was both superficial and deep hyperæsthesia; no contraction in the muscles below the knee to strong faradic stimulation. Complete recovery resulted.

Case 3.—Multipara, 31 years, immediately after confinement complained of difficulty in walking and weakness in her arms. The knee-jerks and superficial reflexes were absent, and the cutaneous sensibility was diminished in her arms and legs. In addition, she had a double ptosis, a divergent strabismus, and a complete internal ophthalmoplegia in both eyes. Her optic discs were normal. After a period of five years the patient's condition was unchanged.

Korsakow and Serbski have described a case with autopsy, in which well-marked degenerative changes were found in the peripheral nerves, especially in the most distal nerves, *e. g.*, dorsalis pedis. The other nerves most affected were the median, ulnar, phrenic, abducens, acoustic, and vagus. In the spinal cord an increase of connective tissue was found in the columns of Goll, and in the lateral columns, especially on the right side. No pathological changes were found in the brain. The patient was 27 years old, and at the fourth month of an extrauterine pregnancy started to suffer from vomiting. The case was complicated by a parametritis, and an abscess in the iliac fossa. She was forgetful, confabulated, had a retention defect, was dull and tearful, and had visual hallucinations. The muscles of the legs and arms were weak, pain was elicited on deep pressure, but the knee-jerks were retained. Her pulse was 140 per minute.

Another case with autopsy has been reported by Solowieff. This case in contrast to most of the others occurred in a primipara. The patient was 24 years old, and at the third month of her pregnancy was in a very poorly nourished condition, owing to persistent vomiting. She became restless, suffered from headache, and paræsthesias of the lower extremities, which were sensitive. She became unable to walk, the knee-jerks were lost, pain was elicited on deep pressure, and the reaction of degeneration was present. Later the diaphragm became weak. Her pulse varied from 130 to 160 per minute. Mentally, she is described as having been delirious and very forgetful. At autopsy degenerative changes were found in the phrenic, peroneal, median, and vagus nerves.

Lunz has described a case in which, owing to an early involvement of the cranial nerves, the similarity of the condition to a diphtheritic paralysis is emphasized.

A woman, 24 years old, gave birth to a weakly child, which died after two weeks. A short time later the patient experienced difficulty in swallowing and choking; then diplopia and dizziness developed. First the right hand felt dull, later the left hand and arm, and later still the lower extremities. Gradually, the swallowing difficulty became worse; slight weakness showed itself in both sixth nerves; slight paresis of the left side of the face, the tongue was protruded to the left, and the palate was not well elevated on phonation. She developed a *main-en-griffe* on the left side, became unable to walk more than a few steps, and pain was elicited on deep pressure of the muscles. The triceps jerk was absent on both sides, but the other tendon reflexes in the arms were retained; the knee-jerks were absent; the electrical excitability was diminished.

One of the most important series of cases (4) has been published by Eulenburg:

Case 1.—One-sided neuritis, with atrophic paralysis in the median and ulnar spheres. The patient was a primipara, 28 years, who ten days after labor experienced severe diffuse pain in the left arm, paralysis and atrophy, which, after a period of two months' treatment with massage, cleared up.

Case 2.—A case of neuritis of the right tibial nerve with subsequent recovery. This case was associated with vomiting.

Case 3.—One-sided neuritis in the region of the right sciatic nerve. The affection started at the end of the first week of the puerperium. This case likewise was associated with vomiting.

Case 4.—A multipara, 27 years, who during her second pregnancy had to have an abortion performed at the fourth month on account of severe vomiting. Eight days later she had the feeling that the lower part of the body was paralyzed. She next suffered from severe pain, and in 24 hours there was complete paralysis of the legs, then paresis of the arms, the back muscles, and finally aphonia and paralysis of swallowing, all in the course of 48 hours. During the course of the next eight days she became insensitive and confused. After several weeks the aphonia and difficulty in swallowing disappeared, the motility returned to the arms in the shoulder and elbow regions, but the fingers and hands, as well as the lower limbs, remained completely paralyzed. Pain was elicited on deep pressure of the muscles; at first there was some superficial sensory disorder, but later very little. The knee-jerks were absent on both sides; the reaction of degeneration was present.

In most of the cases so far referred to uncontrollable vomiting has been a prominent feature, but Elder has reported two cases, neither of which suffered from vomiting.

The patients were multiparæ, and in each the symptoms started about the sixth month of pregnancy. The symptoms started with tingling and paræsthesia, chiefly in the hands, but also in the feet. There was little or no paresis, but sensation was affected in both cases. In both cases alcohol, diphtheria, glycogenia, and lead could be ruled out. After delivery the improvement in both cases was rapid. Butler's case followed delivery, but from the description there can be little doubt about the diagnosis.

A married woman, 37 years, had at the fourth month of pregnancy a still-born child. Three weeks later she developed a "milk leg" on the right side, suffered from vomiting, and started to fall off in weight. Later she lost power in both legs; numbness and tingling developed in the hands and arms, which

was later followed by weakness. On examination there was marked atrophy of all the muscles of the upper and lower extremities, and also of the trunk muscles. The knee-jerks were absent; tenderness was elicited on deep pressure of the muscles. The electrical reactions were impaired. Improvement occurred under massage and general measures.

One of the best and most comprehensive articles on this subject is that of Reynolds, who in 1897 gave a general summing up of the known facts, and described one personally observed case.

Primapara, 24 years, when four months pregnant, was suffering from such severe and uncontrollable vomiting that an abortion had to be procured. Following the abortion, the patient suffered from complete loss of sphincter control for two or three weeks. About a month after the abortion her feet felt cold and numb, and a month later still her legs were very weak, and sensation in them was almost entirely abolished; there was no affection of the upper extremities. Finally, she could not stand or walk; her knees were contracted, and the knee-jerks could not be obtained. The patient improved under massage. Two years later the patient had a successful second pregnancy without vomiting, and without untoward results.

Saenger's six cases are also all interesting, in that they all developed after an apparently normal labor.

CASE 1.—A woman, 36 years, on February 12, 1896, had a normal labor. Previous to the birth the patient had experienced some weakness and tingling in the left arm, and occasionally a feeling of pain. Shortly after the birth a dull feeling, weakness, and some pain developed in the right arm. After some days there was complete paralysis of both arms and legs; pain was elicited on deep pressure over the nerve trunks; the tendon reflexes were absent. Later weakness developed in the diaphragm and back muscles; transitory swallowing difficulty, and rectal paralysis; the bladder was not affected. A partial reaction of degeneration was elicited in the tibialis anticus, and in the peroneal muscles. By Christmas, 1896, the patient was completely well.

CASE 2.—A woman, 30 years, several weeks after a normal labor and puerperium developed an acute generalized polyneuritis of the nature of a Landry's paralysis. There was a transitory rectal paralysis. Sudden death resulted. No changes were found in the cord or brain. A well-marked degenerative neuritis was found in the peripheral nerves, and also in the vagus nerve.

CASE 3.—A woman, 34 years, had a normal labor, and no fever during the puerperium, but developed a dull feeling in her fingers, and then weakness in both legs. There was some pain and tenderness of the bladder. Soon there developed complete paralysis of both the upper and lower extremities, pain was present on deep pressure of the muscles, slight cutaneous sensory disturbance, and absence of the tendon and skin reflexes. The reaction of degeneration was elicited in the small muscles of the hand, and in the calf muscles. Complete recovery resulted after a period of four months.

CASE 4.—A woman, 32 years, five days after labor developed a paresis of the left median and ulnar nerves. The patient recovered in a few weeks.

CASE 5.—A woman, 28 years, ten days after labor developed pains in her legs, and then in the arms. After some days there was a neuro-myositis of the right radial and median nerves; after some weeks the same affection occurred in the left arm, but to a lesser degree. This patient also recovered.

CASE 6.—A case of double-sided retro-bulbar neuritis.

In none of these cases, with the possible exception of the last, was there any suspicion of a febrile process.

Danziger's case is in many ways similar to that of Lunz, and is of interest, owing to the early involvement of the cranial nerves. A primipara, 21 years, 14 days after normal labor experienced difficulty in swallowing. On the next day there was hoarseness, twitching of the face, and general pain. The soft palate was only very slightly raised on phonation, the speech was nasal, and in swallowing fluid was regurgitated through the nose. The right vocal cord was in a cadaveric position. The arms and legs were weak, and pain was elicited on pressure. The knee-jerk was absent on the right, and diminished on the left side. A gradual recovery resulted.

A most interesting case with autopsy has been described by James Stewart. A multipara, 33 years, about two months previous to confinement started to experience numb feelings in her limbs. In the previous pregnancies she had suffered from severe vomiting, and in this last pregnancy the vomiting was so severe that for six weeks she was confined to bed. She was emotional, but otherwise her mental condition is described as normal. About nine weeks after labor she showed considerable loss of power in the muscles of both lower limbs, but in no single muscle, or group of muscles, did it reach an absolute degree; it was distinctly more marked in the most peripherally situated muscles. In both upper limbs a similar, but less marked paralysis was present, being also more marked in the distal parts. There was, however, no definite foot-drop or wrist-drop. The feeling of numbness in the lower limbs and abdomen extended up to the eleventh thoracic segment, and in the arms it extended up to a point midway between the elbow and shoulder. Touch was diminished over the numb areas; pain and thermal sense were unimpaired. The calf muscles were very tender on pressure, the knee-jerks were normal, and the electrical reactions were not disturbed. The pulse was rapid varying from 80 to 120 per minute; the respiration rate was from 24 to 30 per minute. The urine at all times was free from any abnormal ingredients. Later there was complete wrist- and foot-drop, and the knee-jerks became lost. Later still the diaphragm became paralyzed, and death finally resulted from pneumonia.

The examination of the nervous system was made by Dr. Shirress. The brain, spinal cord, and ganglia, were removed; also both sciatics, musculospirals, anterior crurals, peroneals, anterior tibials, pneumogastrics, and phrenics. Microscopically, the peripheral nerves by Marchi's method showed the signs of a true parenchymatous degeneration, the hæmotoxolin and Van Gieson's method revealed also a marked interstitial inflammation, the blood vessels being distended with numerous hæmorrhages in the epi- and endoneurium. The pneumogastric and phrenic nerves showed more of a parenchymatous condition than interstitial changes. In the cord a scattered degeneration was found in the posterior columns. Degenerated fibers were also found in the lateral region of the cord (direct cerebellar tract) in the upper dorsal and cervical segments. The posterior roots were degenerated along the whole length of the cord. No changes were found in the anterior roots.

Marked and advanced chromolytic changes of the peripheral, central, and perinuclear varieties were found in the ganglionic cells of the gray matter in the anterior horns, and in Clark's column. The most marked changes were found in the fifth, sixth, and seventh cervical segments.

Other cases with autopsy reports have been described by Mader and Lindemann. Mader's case was associated with persistent vomiting, and at autopsy extensive neuritic changes were found in the sciatic, tibial, and peroneal nerves; the cord was not involved. In Lindemann's case, in addition to there being a parenchymatous neuritis, degenerative changes were also found in the liver and kidneys. Still another case with autopsy has been reported by Dustin:

A multipara, 30 years, at the sixth month of the last pregnancy suffered from uncontrollable vomiting. Following the birth of a macerated fœtus a quiet delirium set in without fever. She developed pain in the left leg, which became contracted; and lost control of her sphincters. Her pulse varied from 100 to 108, and her breathing was above 30 per minute. The leg muscles became atrophied, pain was elicited on deep pressure, and the knee and Achilles jerks were absent. At the autopsy degenerative changes were found in the crural and sciatic nerves. At the third lumbar segment of the cord there was chromolysis and vacuolation of the anterior horn cells. The anterior and posterior roots were normal.

In 1913 Hahn described a case which clinically was similar to that of an alcoholic Korsakow psychosis:

A multipara, who three years previously in the third month of pregnancy had suffered from severe vomiting, and had two epileptiform attacks. During the last pregnancy vomiting again started during the third month, then nystagmus developed, and the pulse became above 100 per minute. An artificial abortion was performed, which stopped the vomiting, but the general condition of the patient was not improved. The patient became very dull, the nystagmus became more marked, a retinal hæmorrhage occurred, both legs were paralyzed, the patellar reflexes were lost, and there was a sphincter paralysis. All these severer symptoms occurred about 12 days after the artificial abortion.

Mentally, the patient at first was dull and confused, but later a delirious condition developed, in which she thought that she held her baby in her arms, kissed it, and showed it to the other patients. After the acute stage had passed the patient lapsed into a state of mild euphoria with spells of irritability, had an exceedingly poor power of retention, and an amnesia for her hospital residence. In the course of eight months her power of retention showed considerable improvement.

Before concluding this review of the literature, I would just like to mention the cases and communications of Hösslin, Dufour and Cottenot, Stelzner, Burr and McCarthy, Craik, Cross, Buzzard, Aldrich, Borham, Köster, Johannsen, and Bernhardt.

General Considerations.

It is an accepted and well-known fact that the equilibrium of health is more apt to be disturbed during pregnancy than at almost any other time. Wright believes that during pregnancy there is a general systemic toxæmia, due to the more or less faulty action of the liver, intestines, and kidneys, and toxins can be found chiefly in the blood, liver, and muscles. Wright emphasizes the fact that the slightest departure from health during pregnancy should make one suspect a toxæmia, and some of the symptoms he lays stress on are: salivation, disorders of digestion, and constipation, general malaise, anæmia, nervous disturbances with headache, disorders of vision, irritability, deficient urine excretion, and albuminuria. Bouffe de Saint-Blaise (quoted by Hösslin), in considering the toxins of pregnancy, has also emphasized the changes in the liver and kidneys, and his work, of course, is of particular interest in relation to Lindemann's case, where there was not only a parenchymatous neuritis, but also degenerative changes in the liver and kidneys.

Eulenburg, in common with most others, believes that some cases, although only observed during the puerperium, are in reality cases of the neuritis of pregnancy, and he advanced the hypothesis that impaired gastrointestinal functions during the gravid period led to an autointoxication through the formation in the gastrointestinal tract of some substance—possibly acetone—which is absorbed, and causes the neuritis.

Reynolds had the idea that persistent vomiting set up an acetonæmia, and that acetone, or some allied product, produced the neuritis, just as may happen in the neuritis of diabetes. So far, however, no evidence has been produced to substantiate the acetone theory, and we have no knowledge of the nature of "the toxin" which is supposed to be responsible for the condition.

The relation which hyperemesis gravidarum bears to the condition seems to be a close one, especially in those cases which show a generalized type of neuritis. Bayle has even gone so far as to say that the generalized forms only occur after severe cases of hyperemesis, and it was no doubt on account of the same supposition that Clifford Allbutt believed that the vomiting and the neuritis were due to the same toxin. A number of cases, *e. g.*, those of Lunz, Saenger, Korsakow, Danziger, and Elder, have now, however, been described in which no mention is made of the occurrence of hyperemesis gravidarum, and therefore Allbutt's and Bayle's supposition can hardly hold good. But from the very frequency of its occurrence there can be no doubt that hyperemesis plays a most important role, whether or not it is from the hyperemesis *per se*, or from the fact that the hyperemesis is responsible for causing a general exhaustion of the patient, thus rendering the patient more susceptible. Out of 92 cases of all grades of the neuritis of pregnancy collected by Hösslin, hyperemesis gravidarum was present in 19. Hösslin, however, remarks that this number assumes much greater proportions when it is stated that the cases of neuritis which gave a history of hyperemesis were much the most severe. Out of 46 cases in which all the extremities were paralyzed, hyperemesis was present in 16, while in the anamnesis of 37 cases where only the facial nerve, or one, or only the upper extremities were involved, hyperemesis was not reported. According to Hösslin, the fact that the hyperemesis is associated with the more severe cases is proof positive against the hysterical nature of the vomiting, and he conclusively states that he knows of no case of hysterical vomit-

ing in a non-pregnant woman associated with polyneuritis. Since Hösslin's article was published a number of other cases have been reported, *e. g.*, those of Dustin, Dufour and Cottenot, Hahn, and the two which are the subject of this paper, and in all of these cases persistent vomiting seems to have been an important factor.

In addition to the hyperemesis, the weak, exhausted, emaciated, condition resulting from it, the retention of a macerated fœtus, the retention of placenta, and the involution of the uterus, have all been supposed to have played a part. At present, however, we must content ourselves with the summing up of Aldrich, and say that the condition is one which usually occurs in women exhausted from vomiting, and that probably some toxin is formed within the body of the mother or child which has a selective action on the nerve tissue of the pregnant woman.

Another point which may be emphasized is the much greater frequency with which multiparæ are affected as compared with primiparæ, the reaction apparently being in the nature of an anaphylactic phenomenon.

The indications and the time for the production of abortion are questions for the obstetricians, but it may be well to remark that most of the French observers state that when the pulse increases to 100 or over per minute an abortion should be immediately produced. The points, however, which I especially wish to lay stress on are:

(1) The pregnant state must in certain cases be recognized as an important etiological factor in the production of peripheral neuritis, and of that condition known as Korsakow's syndrome.

(2) The neuritis caused may be either (1) local, *e. g.*, affecting one nerve or one limb, or (2) diffuse, *e. g.*, affecting all the limbs, and certain of the cranial nerves.

(3) The mental disorder characteristic of the condition is usually associated with a generalized polyneuritis, but, as evidenced by one case reported here, it may occur alone.

(4) The frequent history of hyperemesis gravidarum in association with the generalized forms of the disorder is so striking that it suggests a possible line of approach as to the elucidation of the nature of the toxin.

(5) Those patients who in previous pregnancies have suffered from severe vomiting, or other serious toxic phenomena, should be strongly urged to avoid any further pregnancies.

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OBSERVATIONS UPON THE BACTERIA FOUND IN MILK HEATED TO VARIOUS TEMPERATURES.

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More than twenty-five years ago Flügge,[1] then Professor of Hygiene in the University of Breslau, pointed out the important fact that milk heated to various temperatures always shows, upon incubation at 22° C. or at 37° C., a bacterial growth due to the presence in the milk of heat-resistant spores. This was equally true of boiled milk or of milk exposed to the lower temperatures employed in pasteurization. Dependent upon the kind of bacteria developing, Flügge differentiated two sorts of decomposition which might occur, one explosive and caused by gas-producing anærobes, and one consisting of a slow liquefaction of the proteids in the milk and due to peptonizing ærobes. To the latter group Flügge attributed particular significance, since the changes produced by such bacteria in the milk were slow and easily overlooked, and yet the milk might be full of microörganisms. He therefore raised the important question as to the rôle which these bacteria might play in the production of the summer diarrhœas of children. Under ordinary circumstances the spore-bearing organisms in milk would be restrained by the growth of the lactic acid organisms and only in milk heated to a temperature sufficient to destroy the latter group could the former group (spore-bearing bacteria) develop in such profusion as to change the character of the milk or offer any danger to children. According to Flügge, the spores of the peptonizing bacteria would resist the action of the acid gastric juice and find the proper conditions for development in the lower bowel, where they would multiply and elaborate the poisonous products which give rise to the grave symptoms of intoxication seen in summer complaint. The various microörganisms isolated by Flügge from heated milk were later studied by Gotschlich and Kaensche. The *Bacillus butyricus* of Hueppe was the principal anærobe and species usually classified as "subtilis" or "mesentericus" forms (*Bacillus subtilis, Bacillus mesentericus vulgatus, Bacillus mesentericus fuscus,* etc.), were the most important ærobes.

This elaborate investigation of Flügge has received little or no attention from American physicians, far less indeed than work of such a fundamental importance deserves. As far as we can learn, there has been no particular effort made to determine whether Flügge's conclusions in regard to the presence of peptonizing ærobic bacteria in milk can be applied to this country, although H. R. Brown[2] in Dr. Theobald Smith's laboratory has described a variety of anærobes which occur in the milk in Boston. Dr. Letchworth Smith[3] also, in the Department of Health in New York, has studied the properties of some two hundred organisms isolated from the milk in that city, but not with the particular object of differentiating between the species found in raw and cooked milk. In the many valuable American studies upon the pasteurization of milk, especially those of Rosenau,[4] Jordan,[5] and Ayers and Johnson,[6] Flügge's work has received comparatively little attention, and yet it is probably the most important single investigation upon this subject that has ever been published. For if it be true that milk always contains bacterial spores capable of resisting a high temperature, even that of boiling, and of giving rise, by their multiplication, to putrefactive changes in the milk, this is a fact of far-reaching importance which should never be lost sight of in any consideration of the problem of pasteurization.

Finally, the contention of Flügge that spore-bearing, peptonizing bacteria play a rôle in the summer diarrhœas of children has never been seriously considered here. The general opinion in regard to this work may be indicated by quoting the opinion of a leading writer in this field who states that "this view (*i. e.*, that spore-bearing bacteria survive pasteurization,) started with the work of Flügge and has gradually lost ground for lack of clinical and laboratory confirmation" (Rosenau[7]).

In view of the importance of this question, both from the theoretical and practical standpoint, we have made the attempt to repeat Flügge's work during the past eighteen months in the hope of determining whether his conclusions are applicable to this country. The samples of milk have been collected in Baltimore and Washington, in all about 129 specimens being studied. The results of the examination of the milk in Baltimore only will be reported in this paper, the Washington samples being reported upon by one of us in another paper.

Technique.

The milk sold in Baltimore may be divided roughly into dipped milk and bottled milk. The dipped milk is sold very

largely in the poorer sections of the city, especially in the small shops and corner groceries. Its content in bacteria is uniformly high, as has been indicated elsewhere.[8] The bottled milk is of a much better character, the bacterial content usually low and a certain proportion is pasteurized, but not, however, under city control.[1] No certified milk is delivered in Baltimore, but a Walker-Gordon milk of exceptional purity is sold very largely. The milk here is obtained from a large area of farming land in Maryland and Southern Pennsylvania.

Altogether 78 samples of Baltimore milk, representing 21 different dairies, were employed in this investigation. The dipped milk was collected in the small shops, transferred to sterile pails or flasks and carried to the laboratory, while the bottled milk was delivered directly in the original containers. Considerable care was exercised to obtain milk from a variety of sources to give results which may be said fairly to represent Baltimore conditions. In consequence, the specimens taken represent nearly every kind of milk sold in the city. All the samples of milk examined were subjected to the same treatment. Flasks, varying in capacity from 250-500 cc., were either filled with the milk up to the neck so that the layer of cream should form a plug and produce anærobic conditions at the bottom or were about half filled so as to offer a wide area for oxygen absorption and give satisfactory ærobic conditions. These flasks were heated on the water bath to various temperatures for varying periods of time, care being taken to immerse them to such a depth as to insure the proper heating of the milk itself. All specimens were immediately incubated without cooling at either 37° C. or at 22° C. Raw controls were always carried along at the same temperature. After the lapse of 48-96 hours, when the bacterial changes had fully developed and the characteristic reactions were seen in the milk, agar plates were poured for the cultivation of the ærobic bacteria and rabbits were inoculated in the ear vein with cubic centimeter quantities for the isolation of *Bacillus ærogenes capsulatus* of Welch and Nuttall (*Bact. Welchii*). No attempt was made to work out the many other anærobes which must be present in Baltimore milk, attention being paid only to the "gas bacillus" as giving us the most convenient method of determining the presence or absence of anærobic putrefaction. This organism was always sought for by the method of rabbit inoculation, the lesions found in this animal being regarded as essential in its identification. In general the extent to which the flasks were filled made no appreciable difference in the reactions shown by samples of milk heated to the higher temperatures, but apparently milk heated to 60-65° C. may undergo a variety of changes, depending upon several factors, of which one is the size and shape of the container. This point was not clear by any means, and is still the subject of study by us. The different controls of raw milk behaved in much the same way, the milk labeled pasteurized showing a fairly high bacterial count and acidifying and clotting normally. These latter specimens have not therefore been given separate consideration. Particular attention was paid to the reactions shown by raw milk, by milk heated to 65° C., to 85° C., and by boiled milk.

[1] Since this work was completed the Commissioner of Health of Baltimore City, Dr. Gorter, has been enabled to employ a force of inspectors for the milk-pasteurizing plants in the city.

Reactions of Raw Milk.

All the samples of Baltimore market milk, both raw and that labeled "pasteurized," when incubated at 37° C. or kept at 22° C., exhibited changes which did not differ from those seen in milk in other localities. Within 24 to 48 hours in the thermostat and 48 to 72 hours usually at room temperature the milk was acidified and firmly clotted. Cultures taken within the first few days revealed as the predominant species the organisms first accurately described by Gunther, Thierfelder and Leichmann, and which are known by several names, such as *Bacterium lactis acidi*,[9] *Streptococcus lacticus* and *Bacterium Güntherii*. As Shippen has pointed out, the latter designation, *Bacterium Güntherii*, was given this species by Lehmann and Neuman [10] and should be retained in accordance with the rules of priority in botanical nomenclature. *Bacillus lactis ærogenes* and *Bacillus acidi lactici* stood next in point of frequency, but were by no means common, while *Bacillus coli* was an exceptional isolation. Pigmented organisms were also rarely encountered. Spore-bearing bacteria were almost never found in plates poured during the first few days.

Rabbits inoculated for the isolation of *Bacillus ærogenes capsulatus* were at first uniformly negative, even when the spores of the organism were present in the original milk and it could be obtained on cultures by subjecting the milk to a temperature of 85° C. (see below). Various methods of isolating it were tried. Rabbits inoculated in the ear vein with 1 cc. quantities of whey and then killed and kept in a warm place did not show the characteristic gas œdema, nor could it be obtained on cultures from the blood stream or from the organs. Transfers of whey in 1 cc. quantities to sterile milk tubes which were then heated to 85° C. and incubated anærobically were also without result, the tubes never revealing the gas bacillus reaction. Finally rabbits inoculated with 1 cc. quantities of whey heated to 85° C. to destroy all vegetative bacteria were likewise negative. It was evident that clotted raw milk does not furnish a medium favorable for the survival and development of the gas bacillus, possibly because of its high degree of acidity or possibly because of the many other organisms present. In our first series of six milks the organism was never obtained from raw milk allowed to clot, no matter what method was used. Later, in a second series of six, it was obtained in two cases when the whey was examined early, within the first 48 or 72 hours. Rabbits inoculated with small quantities, killed and kept at 22° C., exhibited an extensive gaseous œdema of the subcutaneous tissues, gas in the fascias between the muscles, gas bubbles in the heart and larger vessels and the characteristic reaction in the liver, the substance of which was riddled with gas blebs. Smears made from the blood and from the juice of the various organs revealed an encapsulated Gram-positive bacillus and transfers to litmus milk and agar

showed the organism of Welch and Nuttall, usually in pure culture.[11] The survival of the gas bacillus in raw milk allowed to clot was evidently the exception, however, and not the rule.

Aerobic cultures from specimens of milk allowed to stand some days continued to reveal only the lactic acid organisms above mentioned with an occasional *Bacillus coli* or *Bacillus lactis ærogenes*. There was no particular increase of spore-bearing bacteria. Eventually very old milk specimens, kept six to eight weeks, showed an abundant surface growth of molds and pigmented species and some softening of the clot. A definite peptonization did not often occur. Occasionally foul odors developed in this very old milk, arising possibly from the multiplication of *Bacillus coli*.

Reaction at 65° C.

Milk heated to 65° C. for 30-35 minutes and then incubated at 37° C. exhibited a reaction which may be regarded as characteristic. Within 24-48 hours it was rather firmly clotted, but the curd did not seem, as a rule, to be so abundant as that in normal raw milk, and in addition it was riddled with gas bubbles. Immediately after the clot was formed softening of peptonization of this clot set in, the gas bubbles being liberated and the milk being converted into a thin whey in which the curd was eventually completely dissolved.

Sometimes the reaction could properly be described as explosive, so violent was the evolution of gas, but in general the reaction seemed to consist more of a gaseous clotting followed by a rapid peptonization. Kept at room temperature the 65° C. milk revealed almost the same changes as were seen in the samples kept at 37° C., but the evolution of gas was not so marked and the peptonization was somewhat less rapid. The end-products were in all cases the same, however, the milk being converted into a thin watery fluid almost completely devoid of grosser particles of whey. Normal clotting without peptonization was extremely rare in milk heated to 65° C. for this length of time. In a series of 18 samples of milk, it occurred but once, the other 17 samples clotting and completely peptonizing.

Aerobic cultures made the first 48 hours to 72 hours revealed a variety of microörganisms the relationship of which to each other and to the organisms found in raw milk is somewhat difficult to determine. Sometimes the only colonies present were spore-bearing bacteria, even the small pin-point colonies seen with a hand lens developing into such species. These were transferred and identified as accurately as possible with our existing knowledge of the non-pathogenic spore-bearers. They belonged to the groups usually called *Bacillus subtilis, Bacillus mesentericus* and *Bacillus cereus*. In addition a spore-bearing organism which has the property of acidifying lactose and acidifying and clotting milk was obtained on a number of occasions. This will be described later in a paper dealing with the spore-bearing bacteria in milk. At other times the plates showed an abundant development of lactic acid organisms, these being even more numerous than the sporulators. Despite this discrepancy the milk samples went on to complete liquefaction. How far a temperature of 65° C. will destroy vegetative bacteria is by no means clear. In our experience lactic acid organisms survive this temperature in a certain proportion of cases and this has been also the experience of Rogers,[12] Ayers and Johnson, Russell[13] and a number of others who have called attention to organisms which withstand pasteurization.

Bacillus ærogenes capsulatus could not usually be obtained from 65° C. milk, even when the milk showed an explosive reaction. Thus in 12 samples with this reaction the gas bacillus was found by rabbit inoculation in only two instances, in the other ten cases the rabbits showing no gaseous œdema and cultures failing to reveal the organism of Welch and Nuttall. In eight of these ten samples the gas bacillus was present in the milk, the samples heated to 85° C. revealing it in abundance. Thus 65° C. milk, like raw milk, does not offer suitable conditions for the multiplication of this species and the explosive reaction seen in milk heated to this temperature can hardly be attributed to it. What part other anærobes play in the production of the reaction does not, of course, appear from our experiments, nor was it clear whether gas-producing ærobes were not also left behind. On the whole we were inclined to regard the reactions seen in 65° C. milk as due to the combined action of the lactic acid organisms, spore-bearing species, and either gas-producing anærobes other than the gas bacillus or some gas-producing ærobes surviving the heating of the milk. In the hope of clearing up the doubtful points, a number of samples of milk were heated to 60° C. for various periods of time and ærobic cultures taken. The results varied widely. At times the samples of milk clotted normally and cultures revealed only the ordinary lactic acid bacteria with an occasional spore-bearer. At other times the samples showed an explosive reaction like that of 65° C. milk, while the clot which was formed was rapidly peptonized. In general, the reaction consisted of a rapid coagulation of the milk and a slow peptonization of the coagulum. Cultures from such milks revealed many of the sporulating organisms seen in 65° C. milk mixed with the lactic acid bacteria. The reactions in milk heated to 60° C. for 30 minutes did not differ especially from those seen in milk heated to 65° C., but the proportion of samples showing normal clotting was greater. Thus in 18 samples heated to this temperature 14 clotted and completely peptonized and four clotted normally without peptonization. In 12 samples heated to the same temperature for shorter periods of time, 10 and 20 minutes, three specimens clotted normally and here ærobic cultures showed only lactic acid organisms, while nine specimens clotted and peptonized. In general the samples of milk which showed a normal clotting at 60° C. or 65° C. were from better-grade dairies than those in which the clot was peptonized, but this was not a universal rule. The reactions of both 60° C. and 65° C. milk were by no means clear, and it was evident that they might depend upon a variety of factors. The age of the milk, the original bacterial content of the samples, the amount of contamination by spore-bearing bacteria, both ærobic and anærobic, the shape of the container, all might be factors which played an impor-

tant part in determining the end-reaction. In short, milk heated to 60-65° C. is just on the border line and is capable of undergoing a variety of changes. Since this is the temperature of commercial pasteurization, it is hoped that future investigation will clear up some of these doubtful points.

REACTIONS AT 85° C.

Milk heated to 85° C. for 30-35 minutes and then incubated at 85° C. showed the same reaction in nearly all the samples examined. Within 12-18 hours it was firmly clotted and partially peptonized, with the active evolution of gas. The combination of these three changes gave the samples a characteristic appearance, which may properly be designated as violently explosive. The evolution of gas was frequently so pronounced as to force the upper layer or plug of cream out of the flask, the cotton stopper being carried with it and being deposited on the shelf of the thermostat some little distance from the flask itself. By the end of the first day the casein was often completely peptonized and by this time the evolution of gas had also usually subsided. Rarely the complete solution of the coagulum was delayed for 48 hours. Milk which has undergone this explosive reaction has the characteristic odor of butyric acid, which may give way to the disagreeable odor of putrefaction if the samples are kept some time.

This violent gas reaction with coagulation of the milk and complete peptonization may be regarded as typical of milk heated to 85° C. and then incubated at 37° C. It was obtained in all instances in a series of 72 samples of Baltimore milk, regardless of the source. Dipped milk from the corner stores and bottled milk of the better grades alike showed it. Occasional variations in the intensity of the reaction and the length of time required to bring it about were noted, but in all instances the end-result was the same, a complete liquefaction of the precipitated casein.

Aerobic plates made from 85° C. milk at various intervals, both early and late, revealed a host of microörganisms, all of which seemed to belong to the groups of sporulators mentioned above. Among them may be mentioned such species as *Bacillus subtilis, Bacillus mesentericus vulgatus, Bacillus cereus* and the spore-bearing coagulator already referred to. On no occasion did we obtain on our plates any lactic acid organisms or non-sporulating bacteria of other groups.

Rabbits inoculated with small quantities of whey (1 cc.) and kept in a warm place were nearly always blown up by the end of 18 hours and at autopsy showed the gaseous œdema characteristic of experimental inoculation by *Bacillus ærogenes capsulatus* (*Bact. Welchii*). The blood in the heart and larger vessels was permeated with gas bubbles and the liver was decomposed in the typical way. Smears from the blood and organs revealed the Gram-positive encapsulated gas bacillus and cultures on litmus milk and agar were also positive. The gas bacillus is probably always present in Baltimore milk and may be obtained by heating it to 85° C. and inoculating rabbits. In 30 consecutive samples showing the typical reaction rabbit inoculation gave characteristic appearances in the tissues and positive cultures 25 times. In the 5 negative cases the animals were inoculated with milk more than four days old, suggesting that the organisms had died out or been overgrown by other species.

The changes seen in 85° C. milk may thus be said to arise from the combined action of ærobic spore-bearing bacteria and *Bacillus ærogenes capsulatus*. The latter organism is doubtless responsible for the violent evolution of gas and the former organisms for the complete peptonization or liquefaction of the casein, since we know that the gas bacillus does not bring about this change. The study of these samples of 85° C. milk indicates that the spores of ærobes and of the gas bacillus are widely distributed in milk of this vicinity and even suggests that we may be dealing with peculiarly heavy infections of the cow stables or of the dairies with germs of this character. Other anærobes are also undoubtedly present, but our attention was paid chiefly to the gas bacillus, the presence of which may be regarded as universal.

Milk heated to 85° C. for 30 to 35 minutes and kept at room temperature, about 22° C., shows reactions which are slightly different from the reactions seen in 85° C. samples kept at the body temperature. The variations seem to relate to the time at which the changes manifest themselves and not to any qualitative difference in the reaction. Thus in a number of samples kept at room temperature a firm coagulation occurred within 48 to 72 hours. The coagulum was at times permeated with gas bubbles and the appearance was quite like that described above as violently explosive. At other times the evolution of gas was either lacking or so slight as not to be noticeable, the gas bubbles escaping quietly as they were formed. Peptonization of the clot occurred also in all instances. This peptonization was quite slow, requiring 10 to 14 days for its completion, but the end-result was the same in all cases, a complete liquefaction of the casein.

The changes seen in 85° C. milk kept at room temperature are dependent upon the same organisms as are found in 85° C. milk kept at 37° C. Aerobic cultures revealed the usual spore-bearing bacteria and the gas bacillus was isolated in about half the samples first examined. These examinations were made with specimens which had been kept some time, 10-14 days. In a later series examined for the gas bacillus in the first two days positive isolations resulted in all instances.

Milk heated to 85° C. and then kept on ice at a temperature a few degrees above freezing point undergoes no changes visible to the naked eye. Nevertheless the spores of the organisms originally present retain their vitality for some time and when the samples are placed at a higher temperature, 22-37° C., the various species multiply and bring out the characteristic reactions. A number of samples of 85° C. milk kept on ice for 4-6 weeks revealed no changes, and yet when they were incubated in the thermostat they underwent the decomposition characteristic of 85° C. milk.

Finally the length of time during which milk must be exposed to a temperature of 85° C. to bring out the explosive reaction is by no means always 30-35 minutes. An exposure

for 10 minutes and for 5 minutes also suffices to destroy the non-sporulating organisms and permit the development of the ærobic and anærobic spore-bearers. Thus in a series of six samples, in which a positive reaction was obtained at 85° C. in all cases, the same reaction was observed in the samples heated to 85° C. for 10 minutes and for 5 minutes.

Milk heated to 80° C. does not differ essentially from that heated to 85° C. and no particular study was conducted on the effects of this temperature. In a series of six samples, in which the characteristic reaction was obtained in all instances at 85° C., the same reaction was observed in samples heated to 80° C. for 30 minutes and also for 20 minutes. No especial attempt was made to find the exact temperature at which the foul, stinking reaction produced by Bienstock's *Bacillus putrificus* occurs in Baltimore milk. This probably lies between 70° and 80° C.[1]

Reactions of Boiled Milk.

Milk boiled for 30-35 minutes and then incubated at 37° C. exhibits a variety of changes which may also be seen in the samples preserved at 22° C. In general, three reactions may be noted: clotting without subsequent peptonization; clotting followed by peptonization; and peptonization without clotting. The most frequent reaction in Baltimore milk is the second. Thus in a series of 24 samples, 11 showed clotting, followed by peptonization; 7 showed firm clotting without peptonization, and 6 rapid peptonization without clotting. The explosive reaction seen in 85° C. milk is usually lacking. In the above series it occurred but twice in the 11 samples, showing clotting followed by peptonization. Samples of all these milks heated to 85° C. for 35 minutes showed an explosive reaction and *Bacillus ærogenes capsulatus* was isolated from them.

From this series it may be seen that clotting of boiled milk is a more frequent occurrence in Baltimore than the slow peptonization without clotting described by Flügge, since 18 samples in a series of 24 underwent this change. The changes which take place in boiled milk are naturally very slow and the temperature of 100° C. must destroy the vast majority of the microörganisms originally present in the milk. Even when kept at 37° C. the flasks frequently did not reveal any gross changes or abundant bacterial growths for a number of days, while in the samples kept at 22° C. gross changes were not apparent sometimes for two or three weeks. All our samples of milk boiled 30-35 minutes eventually revealed definite changes due to bacterial development, showing that boiling does not suffice under ordinary circumstances to destroy the bacterial spores present in milk. Our observations are thus in strict agreement with Flügge on this point.

Aerobic cultures from boiled milk revealed nothing but spore-bearing organisms of the "subtilis" and "mesentericus" types, together with our spore-bearing coagulator which is evidently the species usually responsible for the clotting of boiled milk in this vicinity. The gas bacillus is generally absent from boiled milk, its spores evidently not resisting the temperature of 100° C. It was found in two instances only in a series of 12 samples tested for it, these two being the milk which have already been referred to as exhibiting an explosive reaction. Rabbits inoculated with these milks showed the characteristic œdema and the smears and cultures were positive. In the other ten rabbits there was no reaction in the blood or in the organs and the smears and cultures were negative. Since the same samples of milk heated to 85° C. underwent an explosive reaction and the gas bacillus was isolated from them, it was evident that the spores of this species survive boiling only in rare instances, possibly in samples of milk richly seeded with them.

Boiling for shorter periods of time does not affect the milk essentially differently from the exposure for 30-35 minutes. Thus in a series of samples boiled 20 minutes, six samples showed a clot without peptonization, four samples a clot followed by peptonization and two samples a peptonization without clotting. In the same milks boiled 10 minutes the changes were practically identical, except that in one instance an explosive reaction developed, followed by peptonization.

Finally, it may be noted that the complete destruction of bacteria in milk probably occurs only when the milk is boiled for long periods of time or steamed under pressure. Flügge has found that the spores of several species resist boiling for six hours. The application of steam under pressure quickly suffices to kill off all the microörganisms. Thus in six samples of milk which showed an explosive reaction at 85° C., autoclaving with a pressure of 20 lbs. for 5, 10 and 15 minutes gave samples of milk which could be kept for months without revealing any changes attributable to bacterial development.

The reactions seen in milk heated to various temperatures may best be illustrated by the following table which gives the results of our final series of experiments. Here it may be noted that the raw milk clotted normally and showed the gas bacillus in two instances only; 65° C. milk showed an explosive reaction in all instances and yet failed to reveal the gas bacillus; 85° C. milk showed an explosive reaction in all instances, both at 37° C. and at 22° C., and revealed the gas bacillus in all cases in which rabbit inoculations were made; boiled milk showed an explosive reaction with positive gas bacillus isolation in two instances, clotted without peptonization in three instances and peptonized without clotting in one instance, the last four being negative for the gas bacillus.

[1] Similar reactions to those described above have been observed by Klein [14] in London milk and have been attributed by him to an organism which he called *Bacillus enteritides sporogenes* and which he regarded as an etiological factor in summer diarrhœa. The reactions originally published by Klein cannot be reconciled with those of a pure culture and in subsequent publications the reactions attributed to pure cultures of *Bacillus enteritides sporogenes* correspond closely to those given by Welch and Nuttall for *Bacillus ærogenes capsulatus*. The proof that Klein's organism is a distinct species cannot in our opinion be regarded as satisfactory. In addition, it may be noted that cultures of *Bacillus enteritides sporogenes* sent to this laboratory some years ago revealed *Bacillus ærogenes capsulatus* mixed with an ærobe.
W. W. Ford.

SIX SPECIMENS BALTIMORE MARKET MILK TESTED MAY 31, 1913.

	Treatment	Preserved at	Reaction	Gas Bacillus
No. I.	65° C.—35 min.	37° C.	Explosive	Negative
	85° " —35 min.	37° "	Explosive	.....
	85° " —35 min.	22° "	Explosive	Positive
	100° " —35 min.	37° "	Clotted	Negative
	Raw control	37° "	Clotted	Negative
No. II.	65° C.—35 min.	37° C.	Explosive	Negative
	85° " —35 min.	37° "	Explosive	.....
	85° " —35 min.	22° "	Explosive	Positive
	100° " —35 min.	37° "	Clotted	Negative
	Raw control	37° "	Clotted	Positive
No. III.	65° C.—35 min.	37° C.	Explosive	Negative
	85° " —35 min.	37° "	Explosive	.....
	85° " —35 min.	22° "	Explosive	Positive
	100° " —35 min.	37° "	Explosive	Positive
	Raw control	37° "	Clotted	Negative
No. IV.	65° C.—35 min.	37° C.	Explosive	Negative
	85° " —35 min.	37° "	Explosive	.....
	85° " —35 min.	22° "	Explosive	Positive
	100° " —35 min.	37° "	Clotted	Negative
	Raw control	37° "	Clotted	Negative
No. V.	65° C.—35 min.	37° C.	Explosive	Negative
	85° " —35 min.	37° "	Explosive	.....
	85° " —35 min.	22° "	Explosive	Positive
	100° " —35 min.	37° "	Peptonized	Negative
	Raw control	37° "	Clotted	Positive
No. VI.	65° C.—35 min.	37° C.	Explosive	Negative
	85° " —35 min.	37° "	Explosive	.....
	85° " —35 min.	22° "	Explosive	Positive
	100° " —35 min.	37° "	Explosive	Positive
	Raw control	37° "	Clotted	Negative

GENERAL CONSIDERATIONS.

From these experiments upon the effect of heat of various degrees upon milk, this effect being determined by a study of the ultimate changes which the milk undergoes, it is evident that most important biological laws involving the relationship of bacteria are involved. Under ordinary circumstances there are bacteria of three general groups in milk, the ærobic non-sporulating organisms, of which the most abundant are the lactic acid bacteria, the ærobic spore-bearing organisms and the anærobes. These are also in most cases spore-bearing. In raw milk the bacteria of the first group, the lactic acid producers, predominate, and as the milk gets old it sours and clots, due to their multiplication. This may be regarded as the most desirable change in milk, since it resembles most closely the changes which take place in the human intestine while the bacteria involved are entirely free from pathogenicity and may even be beneficial when taken into the alimentary canal. The lactic acid organisms moreover, by their multiplication, may almost completely inhibit the ærobic and anærobic spore-bearing organisms present in the milk. Furthermore, raw milk has its own danger signal, since the acid produced as it sours, while harmless, is rather disagreeable in taste, and thus prevents the use of an old milk which might contain harmful ingredients. As milk is heated the various groups of bacteria are affected in different ways. Beginning at 60° C. we have normally a destruction of the lactic acid bacteria. These may not all succumb at this temperature, but the balance of bacterial growth is altered so that spore-bearing organisms begin to develop and gaseous putrefactive changes begin to occur. How frequent a normal clotting is in Baltimore milk heated to 60° C. is not clear, nor have we determined definitely the relation of this clotting at 60° C. to the original character of the milk nor to the method of keeping it. In the majority of instances in the experiments thus far conducted normal clotting is somewhat rare in 60° C. milk and the clotting which does occur is followed by peptonization. Frequently the reaction is explosive in character. In milk heated to 65° C. there is a further destruction of the lactic acid bacteria; the sporulating organisms are more predominant and the changes which the milk undergoes are nearly always explosive and peptonizing. This reaction is not due to the gas bacillus, but probably to other anærobes. As the temperature to which milk is subjected is raised to 85° C. the lactic acid organisms are entirely destroyed, and the gas bacillus (with other anærobes) develops, giving rise to an explosive reaction with butyric acid as one of the main products. At the same time the ærobic spore-bearing organisms appear in great profusion and variety, converting the curd produced by the gas bacillus or other organisms into a thin, slimy liquid with eventually the disagreeable odor of putrefaction. This change must be regarded as the most undesirable change in milk, since by it the milk is rendered unpalatable and its food value probably destroyed. It must also be remembered that milk heated to 85° C. will explode and decompose even when kept at room temperature, and that the spores which bring about this change survive for a long time on ice. Furthermore an exposure of milk to 85° C. for only 10 minutes suffices to bring about this change in the character of the organisms present in the milk. As the temperature to which milk is heated is still further raised to 100° C. the bacteria which give rise to the explosive putrefactive reaction are destroyed in a short space of time and a new set of reactions is seen in the milk. Boiled milk rarely explodes, but either clots or slowly peptonizes. Finally the complete destruction of the bacterial spores in milk is only accomplished by subjecting the milk to the action of steam under pressure. All these reactions should be kept clearly in mind when working out the scientific principles of milk pasteurization. It may be possible to determine just what the underlying factors are which permit a clotting of milk heated to 60-65° C. and on this devise methods for the pasteurization of milk which will not do way with its capacity of normal coagulation. Heating milk to temperatures above 65° C. in the hope of surely exterminating pathogenic bacteria is of itself a dangerous procedure, since the milk is thus converted into a material in which bacterial development with the production of noxious products is almost certain to occur with the lapse of time. If milk must be heated to over 65° C. to destroy infectious material it should be boiled, since in that way the danger zone of milk heating, ranging from 65° to 85° C.,

may surely be avoided. Finally if such a beautiful antagonism exists in milk between the lactic acid organisms and the spore-bearing ærobes and anærobes, a similar antagonism may exist also in the intestinal tract of man. If this be so, the use of cultures of lactic acid bacteria in intestinal derangements due to the growth of spore-bearers would be advisable while the employment of milk in which the lactic acid organisms are destroyed would be contra-indicated.

From the various experiments reported in this paper we feel justified in drawing the following conclusions:

Conclusions.

1. As first pointed out by Flügge, milk always contains the heat-resistant spores of ærobic and anærobic bacteria, which, by their development, can give rise to disagreeable and unwholesome changes in milk, converting it from a food of great nutritive value into an undesirable if not a dangerous article of diet.

2. These changes take place in milk heated to any temperature from 65° C. to 100° C. and kept at any temperature from 22° C. to 37° C., but not at that of the ice box, 4°-6° C.

3. The spores of the bacteria causing these changes survive in milk for long periods of time on ice and can initiate the same changes in milk kept on ice when transferred to higher temperatures.

4. There is a danger zone in the heating of milk which may be described as ranging from about 65° C. to 85° C. in which milk will never clot normally. Below this temperature heated milk may clot normally. Above this temperature milk will either clot or slowly peptonize.

5. The problem of pasteurization of milk must be worked out on the basis of the changes which occur in milk heated to 60°-65° C. and the result may depend upon the original character of the milk, upon local bacterial infections of milk, on the character of the stables in which the milk is first obtained, upon methods of preservation or upon unknown factors. Further investigation alone can determine these points.

6. With our present knowledge as to the difficulty of getting milk free from pathogenic organisms the safest milk is that which has been boiled for a time varying from ten minutes to half an hour and then preserved on ice. In such milk the organisms giving rise to explosive and putrefactive changes are destroyed, while the organisms which remain usually coagulate the milk or coagulate it and then peptonize it. Rarely they peptonize it without coagulation. While these bacteria may give rise to severe derangements of metabolism in children, and even to disease, as Flügge maintains, this has not yet been clearly shown clinically. Danger from them may probably be almost entirely eliminated by keeping the milk on ice from the time of boiling till the time of use.

7. Milk heated to any temperature from 60° C. to 100° C. must be kept on ice, since heated milk is far more apt to decompose than raw milk.

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ON THE PRESENCE OF SPORE-BEARING BACTERIA IN WASHINGTON MARKET MILK.[1]

By James C. Pryor, M. D.

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Washington market milk at the present time is sold under fairly strict sanitary supervision, owing chiefly to the extensive campaign in that city against typhoid fever, during the course of which it was shown that this disease could be traced in many instances to a contaminated milk supply. In consequence, the conditions under which the milk is handled in Washington have been greatly improved during the past few years. The sale of dipped milk, while permitted, has almost ceased. Most of the milk is bottled and is usually preserved in the retail establishments on ice. Much of the bottled milk is pasteurized at a temperature of 60°-65° C. for 25 to 30 minutes. During the course of this study 51 samples of market milk were examined, 24 of which were raw milk from 17 different dairies, while 27 were commercially pasteurized milk from 8 different sources. A number of samples of the better grades of milk, such as that coming from the Walker-Gordon farms, were also included in this series, so that prac-

[1] Being the synopsis of a thesis submitted to the Board of University Studies, Johns Hopkins University, for the degree of Master of Arts.

tically every variety of milk was represented. The results obtained do not differ materially from those found by Ford and Pryor in their study of Baltimore milk and show that the conclusions reached by those authors apply to Washington as well as to Baltimore. Thus in 30 consecutive samples of milk heated to, and held at, 85° C. for 30-35 minutes, and incubated at 37° C., an explosive reaction with gas evolution occurred almost without exception and a complete liquefaction of the proteids in the milk was observed in every instance. In 27 of these 30 samples the *Bacillus ærogenes capsulatus* of Welch and Nuttall (gas bacillus) was obtained by rabbit inoculation of one cubic centimeter quantities by the classical method, the animals showing the usual reactions in the blood and in the various organs, particularly the liver, characteristic organisms being cultivated from the blood stream. In the three negative instances the characteristic reaction was lacking from the liver and the organism was not obtained on cultures, but bacteria resembling the gas bacillus were observed in smears from the tissues in one case. It is evident therefore that this organism is practically a constant inhabitant of the milk in Washington (27 out of 30 cases = 90 per cent) and can be demonstrated if proper methods be employed. This series of 30 samples includes both raw and commercially pasteurized milk. Controls of unheated milk placed in the thermostat at 37° C. showed in all instances a normal coagulation. Specimens of the same milk to the number of 26 heated to 85° C. and then kept on ice at a temperature of two to three degrees above the freezing point showed no gross changes in periods of time varying from two weeks to two months, but in all instances when transferred to the thermostat at a temperature of 37° C. underwent the same changes as the original 85° C. samples; namely, coagulation, gas production and complete liquefaction. The spores of the organisms giving rise to this reaction are thus capable of surviving long periods of time at low temperatures and give rise to the characteristic changes when placed at a temperature suitable for their development.

Another series of samples of Washington milk was examined for the presence of ærobic spore-bearers. This series included twelve samples of commercially pasteurized milk and nine samples of raw milk. Each specimen was divided into four parts, one heated to 65° C., one to 85° C., one boiled, one preserved as an unheated control. After incubation at 22° C. to 37° C. for periods of time varying from 48 to 72 hours in order to insure a full development of the bacteria present in milk, plates were poured and various colonies picked up and identified. All the raw controls clotted normally and cultures showed the usual lactic acid bacteria with but few sporulating organisms. Of the samples heated to 65° C. but one specimen showed a normal clot. Eleven samples exhibited an explosive reaction with coagulation and gas evolution followed by peptonization, while nine specimens underwent coagulation followed by a peptonization. Aerobic cultures taken from these specimens showed only spore-bearing organisms, except in the one sample which clotted normally and in which lactic acid organisms developed on the plates. These spore-bearers belonged in general to the group of peptonizing gelatin liquefiers, but a number of cultures of the organism mentioned in the previous paper of Ford and Pryor, which acidify and coagulate milk, were also obtained. It would seem therefore that a normal clotting of Washington market milk heated to 65° C. is extremely rare and that this temperature applied for 30-35 minutes under laboratory conditions suffices to destroy the lactic acid bacteria normally present or at least so to inhibit them or reduce their numbers as to permit an abundant development of spore-bearing organisms. Furthermore, a clotting of 65° C. milk does not of itself indicate the survival of the true lactic acid organisms, since there are definite species of spore-bearing bacteria which have the property of fermenting lactose to an acid reaction and acidifying and coagulating milk. How far this conclusion holds true for commercially pasteurized milk is not clear. The various specimens of Washington market milk labeled "pasteurized" which we have had the opportunity of studying clotted normally when preserved at 37° C. or at 22° C. and did not differ in any particular from ordinary raw milk. Plates poured from this commercially "pasteurized" milk furthermore revealed only the lactic acid bacteria characteristic of raw milk. A serious question is raised therefore as to what significance the term "pasteurization" has in regard to Washington milk and to what temperature such milk actually has been raised.

The samples of milk heated to 85° C. showed an explosive reaction with peptonization in 12 instances, in 9 cases a clot being produced followed by a peptonization. Cultures made from these samples revealed only spore-bearing species of much the same general type as those found in 65° C. milk, but no lactic acid bacteria were found on the plates. Several representatives of the acid-producing milk-coagulating spore-bearer previously mentioned were encountered, together with the peptonizing species usually present in 65° C. milk.

Finally the specimens of boiled milk showed an explosive reaction in a much larger proportion of cases than did the Baltimore samples, this reaction being found in 7 cases out of 21. The other samples clotted and slowly peptonized, except in one instance, where the boiled milk suffered no change. Plates poured from all the specimens which showed gross reactions revealed an abundant growth of spore-bearing species which belonged in general to these groups: first, organisms which liquefy gelatin and produce no special changes in litmus milk; second, organisms which liquefy gelatin and peptonize litmus milk with an alkaline reaction; third, organisms which liquefy gelatin, acidify and clot litmus milk and then very slowly dissolve the coagulum.

From this series of 21 samples it is evident therefore that ærobic spore-bearing organisms are widely distributed in Washington market milk and that it is practically impossible to find specimens which do not reveal them when proper methods for their isolation are applied.

CONCLUSION.

From the study of over fifty samples of Washington market milk representing fairly accurately the different kinds of milk sold in the city, we are able to confirm Flügge's original observation as to the presence of spore-bearing bacteria. In our experience the most important anærobic species is *Bacillus ærogenes capsulatus*, which we believe to be universally present. Aerobic spore-bearing bacteria are also found in practically all samples, such organisms belonging in general to the group of gelatin liquefiers. Such species do not develop normally in raw milk nor in the milk sold in Washington as "pasteurized," only the ordinary lactic acid bacteria being found. All these spore-bearing organisms have a profound effect upon milk and when their development is not hindered by the lactic acid bacteria will produce changes of decomposition and putrefaction, rendering the milk unfit for food. How far they play a rôle in clinical conditions, especially in children, remains to be proved.

THE ACTION OF POTASSIUM AND SODIUM IODIDES AND OF THE IODINE ION ON THE HEART AND BLOOD VESSELS.*

By David I. Macht, M. D.

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The iodides, and more particularly the iodides of potassium and sodium, occupy an important place in all pharmacopœias. They have been advocated on purely empirical grounds, in a great many conditions. Their administration in the later stages of lues, in imperfectly understood rheumatic and neuralgic conditions, in various forms of asthma, bronchitis, cirrhosis, and in almost every form of obscure disease is familiar to all.

The rationale and the scientific basis of this usage, however, are very inadequate, and more exact knowledge of the action of these drugs is very much needed.

Among the commonest indications for the use of the iodides are said to be certain cardio-vascular conditions, namely, aneurism and arteriosclerosis. What their action is in such cases is not very clear. According to some [1] they are supposed to promote absorption and to prevent the formation of connective tissue, though this has never been proven. According to others [2] the circulation is improved chiefly through a decrease in the viscosity of the blood produced by the drugs.

Still others [3] ascribe to the iodides a lowering of the blood pressure. Thus Huchard attributes to the iodides the power "to lower arterial tension, to render more active the nutrition of organs, to effect resolution of degenerative processes in the vessel walls, and to lower peripheral resistance." [4]

This effect of the iodides on the blood pressure attracted the attention of numerous observers, mostly clinicians, but there is still no unanimity of opinion on the subject. Potain [5] was one of the first to extol this virtue of the iodides in lowering the blood pressure, which he thought was brought about by their action on the heart and vasomotor nerves. Chelmonski [6] is so sanguine as to the pressure-lowering effect of the iodides that he urges their use in internal hemorrhage, and recently Lucibelli [7] advocated their use in hypertension. On the other hand, other clinicians, as Romberg,[8] Kraus,[9] and Mackenzie,[10] do not note any influence on the arterial lumen or on the heart.

In animal experiments the findings of different observers are also widely different. Sée and Lapique [11] noted after intravenous injections of potassium iodide first a rise and then a fall of blood pressure, which they oddly enough explain by saying that potassium stimulates the heart in a manner comparable to digitalis, and iodine causes a dilatation of the vessels. Huchard and Eloy [12] obtained a marked *fall* in blood pressure from administration of potassium iodide to rabbits, but only after large doses. Prévost and Binet [13] failed to obtain any effect on arterial pressure from moderate doses, while excessive doses produced a fatal fall. Barbera [14] reported a slowing of the pulse and fall of blood pressure in animals after large doses of sodium iodide, which he attributed to a paralysis of the depressor nerves of the heart. Gumprecht [15] in a large series of experiments on rabbits concluded that small and large doses of iodides were without influence on the pressure; that only extremely large doses endangering life cause a fall in tension; and that neither a local action on the vessel wall nor a paralysis of the vasomotor center could be demonstrated. Finally, Stockman and Charteris [16] state that after administering the iodides to patients in doses of from 15 to 40 grs. per day for many days, and in all kinds of normal and pathological cases, they noted no effect on the blood pressure. In animal experiments, according to these authors, when administering NaI or KI by mouth no effect was observed; after intravenous injections, however, while NaI had no effect, KI caused depression of the heart, which was sometimes fatal.

On reviewing the work of the above observers, it would seem that their aim was primarily to ascertain the action of the iodides as such, no special attention being paid to the relative pharmacodynamic rôles played by their constituent parts, namely, by the iodine and the potassium or sodium. The present research was accordingly undertaken especially with a view of determining just how the constituent elements of the salts KI and NaI act on the heart and blood vessels, individually and in combination with each other.

It is perhaps also well to state definitely here at the beginning of the paper, that though the action of potassium, sodium, and iodine in this research is often referred to as an "ion" action, such expressions as potassium ions, sodium ions

*Paper read at a meeting of The Johns Hopkins Hospital Medical Society, May 18, 1914.

and iodine ions are employed more for convenience of description in accordance with the common usage of recent writers, rather than as an attempt to explain exactly how those elements produce their effect on the individual living cells. All that we do know is that K, Na, and I ions are present in the solutions used; but whether those ions act directly as such or indirectly through some intermediary physical or chemical process is left an open question. Indeed there are authors who are inclined to the view that the iodine action is a molecular action,[17] and the fact that in our experiments, as will be seen later, elementary iodine in solution acted in a manner similar to the other iodine effects described in this paper, would tend to lend support to this view.

METHOD.

A normal Locke's solution was made, and then modifications of it were prepared containing the substance, the action of which it was desired to test. These solutions were used in perfusing the blood vessels of cold and warm blooded animals, in perfusing amphibian and mammalian hearts, in studying the behavior of excised arterial rings and strips and in blood pressure experiments. In all cases controls with normal Locke's solution were made.

Normal Locke's solution was prepared according to the following formula:

$CaCl_2$	.....0.024 per cent (crystals)
KCl	.....0.042 per cent
$NaHCO_3$	..0.030 per cent
NaCl	.....0.900 per cent
Dextrose	...0.100 per cent

For convenience of preparing this solution three stock solutions were made as follows:

Solution A.		Solution B.		Solution C.	
$NaHCO_3$	3.0 gm.	NaCl	90 gm.	$CaCl_2$	2.4 gm
KCl	4.2 gm.	Water	1000 cc.	Water	100 cc.
Water	100 cc.				

To make one liter of Locke's solution 10 cc. of A, 100 cc. of B, and 10 cc. of C are mixed with 900 cc. of water and 1 gm. of dextrose is dissolved in the mixture. In order to study the action of the potassium, part of the NaCl in normal Locke was replaced by its *equimolecular* weight of KCl. Thus, for instance, by substituting 2.6 gm. of KCl in place of 2 gm. of NaCl in a liter of normal Locke solution, a solution differing from normal Locke solution only in containing a larger number of K ions, is obtained. By substituting 4 gm. of NaCl by 5.2 gm. of KCl, another solution of greater C_K (concentration of K ions) is obtained.

In order to get at the action of the iodine ion, substitutions of the normal KCl in part or wholly by its equimolecular quantity of KI were made. To obtain a still greater C_I (concentration of I ions) part of the normal NaCl instead of the KCl was replaced by its physico-chemical equivalent of NaI.

In a similar manner other substituted Locke's solutions were made.

I have also experimented with solutions of elementary iodine in normal Locke solution; and various other solutions to be described later.

EXPERIMENTS IN PERFUSION OF BLOOD VESSELS.

The vessels of the hindlegs of a frog were prepared by a modification of the Laewen-Trendelenburg method. The inflow cannula was inserted in the abdominal aorta above its bifurcation, the perfusion fluid being injected at a pressure of 35 cm. and the drop outflow from the veins of the legs being registered automatically on a revolving drum. The results of the experiments were as follows:

The iodine ion markedly increases the vascular tone or constricts the frog's vessels.

The potassium ion causes a relaxation or dilatation of the frog's vessels.

The sodium ion has very little or no effect, and if anything, *increases* the vascular tone.

The effect of injections of the salts KI and NaI is a combination of the effects of their component ions. Sodium iodide causes distinct constriction or increase in the vascular tonus of the frog's vessels. Potassium iodide produces either no effect or a very slight increase in tone, thus indicating that the iodine effect balances and even over-balances the action of the potassium ions. It is well to mention that this depressing effect of potassium on the vessels of a frog has been shown previously, though not on strictly physico-chemical lines, by Hooker.[18] That author studied the effect of Ringer's solution as compared with that solution minus the *whole potassium salt*. For the sake of comparison I have also perfused the vessels with a weak solution of *elementary iodine*, and with a weak solution of hydriodic acid. The elementary iodine in weak solution (1 to 14000), also produces a contraction of the vessels. Hydriodic acid paralyzes the vessel walls (hydrogen ion) and causes a marked increase in outflow.

Having studied the action of the K, Na, and I ions on the frog's vessel walls, it was desirable to ascertain their action on the vessels of a warm-blooded animal, for although the action of drugs on the vessels of a mammal is generally the same as on those of the frog, still it is not always the same. Gunn,[19] for instance, has shown that some substances, namely, quinine, yohimbine, and apocodeine, while acting as vaso-dilators on higher animals, bring about a constriction of the frog's blood vessels. I have, therefore, tested the effect of my solutions on the mammalian blood-vessels, by the ingenious method employed by the Russian investigator, Pissemski,[20] namely, that of perfusing a rabbit's ear.*

This interesting method was employed by us previously in another research.[21] It is simple, though requiring some practice. A needle or cannula is inserted in the central artery of an amputated rabbit's ear, and oxygenated fluid is perfused through it, the outflow from the veins being recorded as in the case of a frog. At a constant room temperature the normal

* In all the experiments on animals, great care was taken to have them completely anæsthetized before performing any operation.

outflow is very constant, and if the perfusing fluid is left at the same temperature the results are quite reliable.

Perfusion of a rabbit's ear gave the same results as in the case of a frog. Iodine ions caused marked constriction, while potassium ions produced dilatation of the vessels.

The findings mentioned above are illustrated by the following protocols and tracings:

EXPERIMENT I.

PERFUSION OF FROG'S HIND LEGS.

Normal Locke Solution.			Outflow 9 drops per 30 secs.					
Inject 10 mg. KI.								
1	minute	later	"	8	"	"	"	"
3	"	"	"	7	"	"	"	"
5	"	"	"	7	"	"	"	"
10	"	"	"	8	"	"	"	"
15	"	"	"	8	"	"	"	"
30	"	"	"	8	"	"	"	"

EXPERIMENT II.

PERFUSION OF FROG'S HIND LEGS.

Normal Locke Solution.			Outflow 8 drops per 30 secs.					
Inject KI 10 mg.								
1	minute	later	"	7	"	"	"	"
3	"	"	"	7	"	"	"	"
5	"	"	"	7	"	"	"	"
10	"	"	"	6	"	"	"	"
15	"	"	"	7	"	"	"	"
30	"	"	"	7	"	"	"	"

EXPERIMENT III.

PERFUSION OF FROG'S HIND LEGS.

Normal Locke Solution.			Outflow 14 drops per 30 secs.					
Inject 10 mg. NaI.								
30	seconds	later	"	14	"	"	"	"
1	minute	"	"	10	"	"	"	"
2	"	"	"	8	"	"	"	"
3	"	"	"	8	"	"	"	"
5	"	"	"	8	"	"	"	"
10	"	"	"	9	"	"	"	"
15	"	"	"	10	"	"	"	"
30	"	"	"	12	"	"	"	"

EXPERIMENT IV.

PERFUSION OF FROG'S HIND LEGS.

Normal Locke Solution.			Outflow 7 drops per 30 secs.					
Inject 1 cc. of elementary iodine in normal Locke (1 to 14000).								
2	minutes	later	Outflow 5 drops per 30 secs.					
5	"	"	"	4	"	"	"	"
10	"	"	"	4	"	"	"	"
15	"	"	"	4	"	"	"	"
20	"	"	"	4	"	"	"	"
30	"	"	"	5	"	"	"	"

EXPERIMENT V.

PERFUSION OF FROG'S HIND LEGS.

Normal Locke Solution.			Outflow 7 drops per 30 secs.					
Inject 1 cc. HI dil. (0.1%).								
1	minute	later	"	8	"	"	"	"
2	"	"	"	10	"	"	"	"
5	"	"	"	11	"	"	"	"
10	"	"	"	11	"	"	"	"
15	"	"	"	15	"	"	"	"
30	"	"	"	15	"	"	"	"

See figs. 1 and 2.

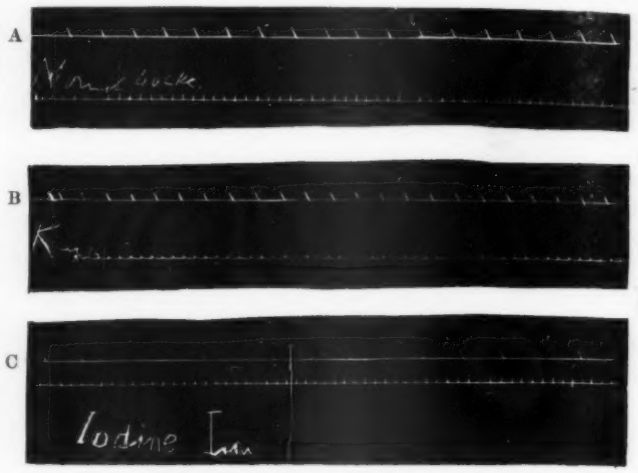

FIG. 1.—Perfusion of rabbit's ear.

A.—Normal Locke; 10 drops in 30 secs.
B.—"K ion" Locke; 13 drops in 30 secs.
C.—"I ion" Locke; 8 drops in 30 secs.
B = Locke with 2 gm. of NaCl replaced by 2.6 gm. KCl per liter.
C = Locke with 2 gm. of KCl replaced by 4.4 gm. KI per liter.

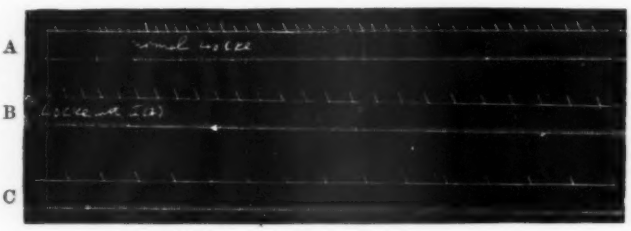

FIG. 2.—Perfusion of frog's vessels, showing effect of iodine ions.
A.—Normal Locke.
B.—5 min. after injection of iodine ions.
C.—10 min. later.

ACTION ON ARTERIAL STRIPS.

The action on arterial rings or strips was studied according to a modification of the original method of O. B. Meyer,[22] and is the same as was used by Dr. Voegtlin and myself[23] on the coronary artery and in my work on the pulmonary.[24] Rings or strips of the carotid, the coronary, the external iliac, and the pulmonary arteries of the ox and the pig were employed. These were suspended first in normal oxygenated Locke's solution at 37° C., and then the normal Locke solution was replaced by the modified solutions already described. It was found by this method also that the potassium ion causes a relaxation of the vessels, and the iodine ion a marked constriction. The action of KI as such is a combination of these two effects, but whereas in the case of perfusion of the frog's vessels, the iodine effect seems to predominate and there is a slight tendency to a diminution of outflow, that is, to increased tonicity, in case of the warm-blooded animals the vessels seem to be more sensitive to the potassium ions and there is a tendency to depression of tone or relaxation. This is especially true of the coronary

arteries, where marked relaxation was noted. On the pulmonary artery potassium iodide showed no effect (Figs. 3 and 4).

ACTION ON THE FROG'S AND THE MAMMALIAN HEART.

The effect on the frog's heart is very striking, as may be seen from the illustrations. It was found that the potassium

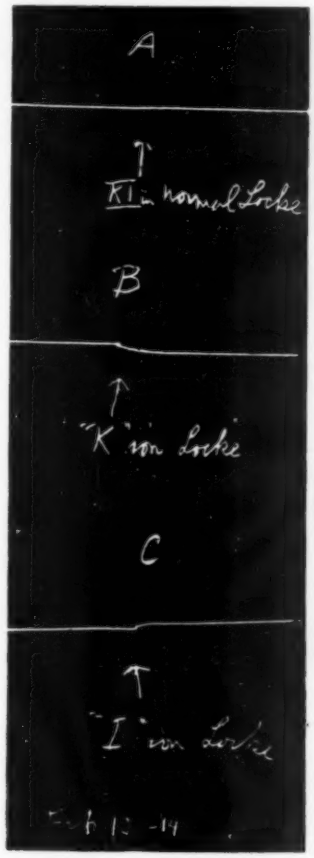

FIG. 3.—Pig's ext. iliac artery; 3 strips, size 10 mm. by 3 mm. each; stretching wt., 30 gm.; lifting wt., 11 gm.
A.—Effect of 1 per cent sol. KI in normal Locke. No effect.
B.—Effect of Locke with half of the NaCl substituted by equimolecular quantity of KCl. "K ions" produce relaxation.
C.—Effect of Locke with half of the NaCl replaced by equimolecular quantity of NaI. "I ions" produce contraction.

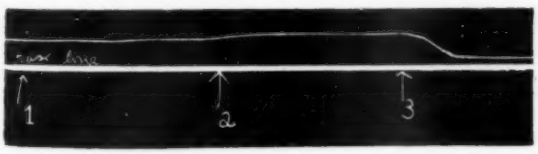

FIG. 4.—Ox coronary, 5 rings; stretching wt., 60 gm.; lifting wt., 40 gm.; speed of drum, 12 hrs.
1.—Normal Locke.
2.—"I ion" Locke = Locke with 2 gm. KCl replaced by 4.4 gm. of KI per liter.
3.—KI 20 ing. in normal Locke.

ion, as has been well known, has a very depressing action, causing speedy standstill in diastole. The iodine ion on the other hand is an active stimulant. The sodium ion has also a slightly

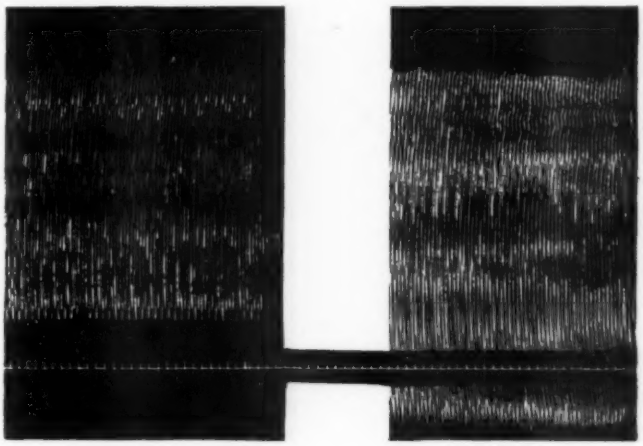

FIG. 6.—Perfusion of cat's heart; Martin's method; showing increase in force of beat and in volume output. Downstroke = systole.
A.—Normal Locke. Output = 10 cc. in 30 secs.
B.—Effect of "iodine ions." Locke with KCl replaced by KI. Output = 15 cc. in 30 secs.

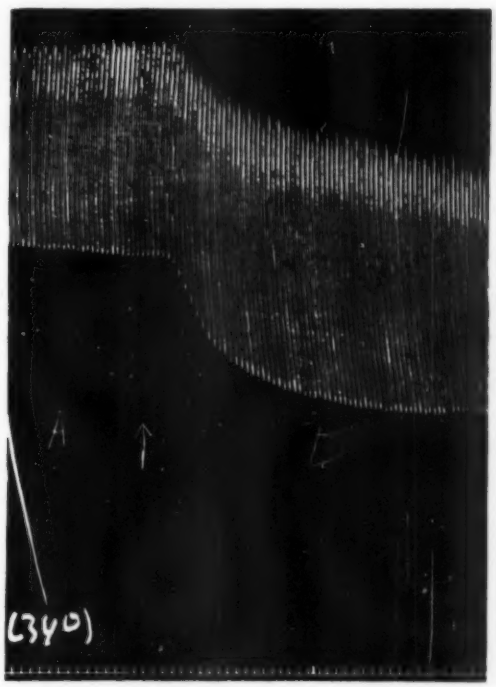

FIG. 7.—A.—Normal Locke. Downstroke-stystole.
B.—Locke with KI in place of KCl.
Cat's heart. Perfusion by Martin's method; showing increase of tonicity and force of beat caused by iodine ions. Downstroke = systole.

tonic effect on the heart. The action of sodium and potassium iodides can be easily explained by bearing in mind the component factors. Sodium iodide containing no depressing factor produces stimulation. Potassium iodide on the other hand shows the predominating influence of the potassium ions, so that weak solutions of KI produce a slowing and weakening of the beat, and stronger solutions arrest the heart altogether (Fig. 5).

In order to corroborate the above findings a series of experiments were also made with a new Locke's solution, which we may term "acetate" Locke solution. This was prepared exactly like ordinary Locke solution, with the exception of the

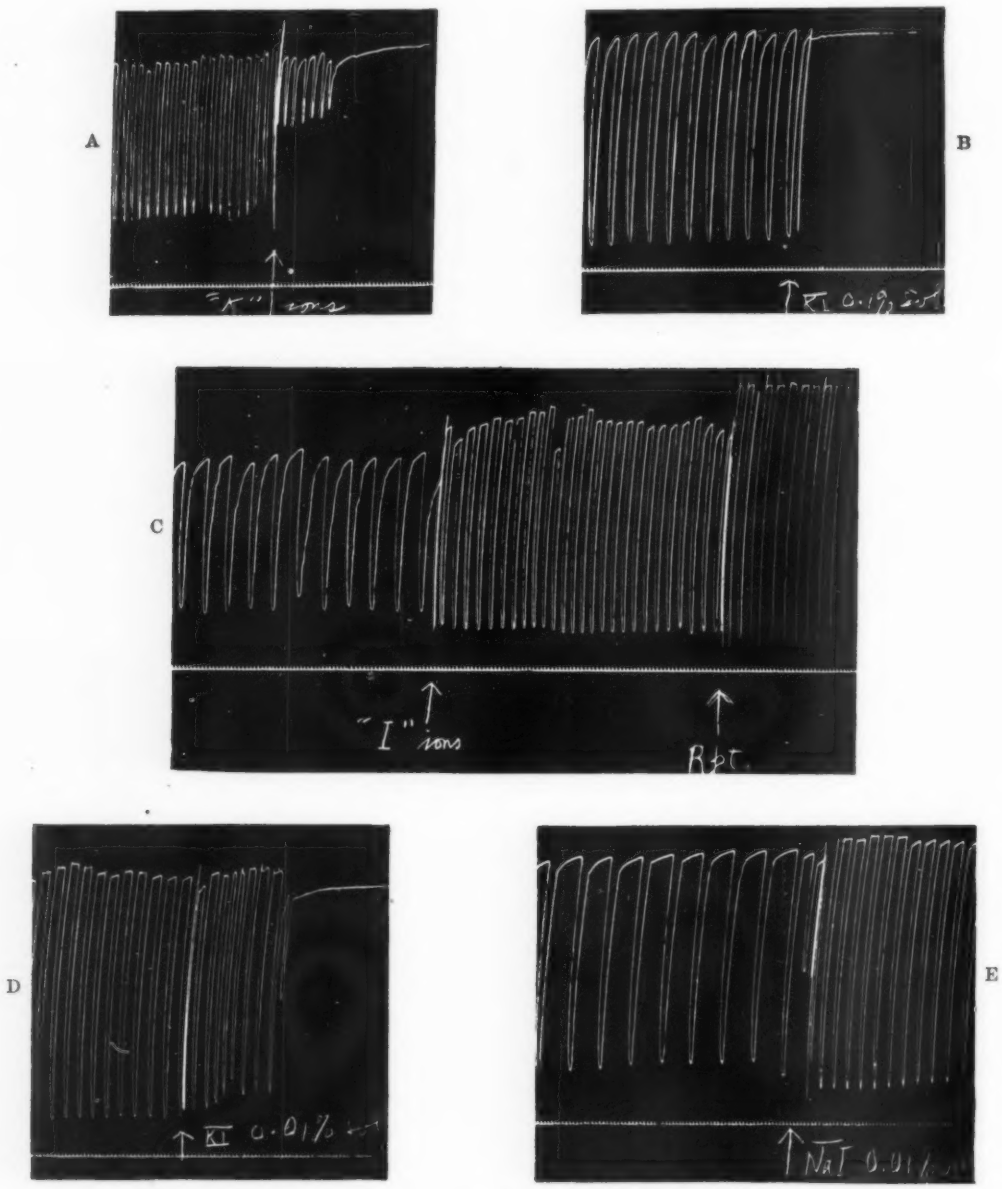

FIG. 5.—Perfusion of frog's heart; suspension method. First part of each tracing is the effect of normal Locke. Arrow indicates introduction of substance tested. Downstroke = systole.

A.—Effect of K ions = Locke with half of NaCl replaced by equimolecular quantity of KCl.

B. and D.—Effect of KI dissolved in normal Locke = combined effect of K and I.

C.—Effect of iodine ions = Locke with half of NaCl replaced by NaI.

E.—Effect of NaI dissolved in normal Locke = combined effect of Na and I.

sodium bicarbonate. Instead of $HNaCO_3$, an equivalent amount of sodium acetate was substituted. Such an acetate solution acts on the heart just as well as and even better than ordinary Locke's solution. Using this acetate solution as a standard, substitutions of it were made to show the effect of K or I ions. Here, too, it was found that potassium depresses, while iodine stimulates, the heart.

Finally, the effect on a mammalian heart was studied by perfusing cats' hearts, by Martin's method. Here again potassium caused depression and iodine stimulation of the heart. Potassium iodide produced depression. The tracings show well the increase in the force of the beat and volume-output, and also the greater tonicity produced by iodine ions (Figs. 6 and 7).

Effect on Intact Animals.

To complete the study of the action of the iodides as such and of their constituent elements, observations were made on blood pressures in intact animals, and here a very interesting phenomenon was noted.

Normal Locke solution injected in quantities of 5 cc. per kilo weight of animal (dog) produced no appreciable change in blood pressure. Sodium iodide and potassium iodide injected as salts dissolved in normal Locke solution in small doses also showed no effect. Larger doses of sodium iodide, 100 mg. per kilo at a time, produced no effect or a slight tendency to a rise in blood pressure. Potassium iodide, however, in doses of 100 mg. per kilo, produced a marked *fall* in blood pressure. This fall in blood pressure after KI was due to the effect of the potassium ions, for it was found that 5 cc. per kilo of a substituted normal Locke solution, containing 0.50 per cent of KCl, in place of 0.40 per cent of NaCl, injected into a dog's vein produced a fall of from 10 to 20 mm. of mercury.

When, however, we studied the action of an "iodine" Locke solution, that is, the action of iodine ions on the blood pressure, contrary to our expectations no rise in blood pressure could be noted. Thus, for instance, 5 cc per kilo of a substituted normal Locke solution containing 1.04 per cent of NaI in place of 0.40 per cent NaCl injected intravenously into a dog, produced no rise in blood pressure. On repeated injections of the same solution a slight increase in the force of the heart beat was observed, and the pressure rose some 5 to 10 mm., but this effect was of short duration, and was by no means as striking as the powerful vaso-constriction and cardiac stimulation produced by iodine ions on isolated organs.

The explanation of this anomalous action was cleared up in a simple manner.

Many years ago Rudolf Boehm,[3] in studying the toxicity of iodine, noted that considerable quantities of iodine could be injected into an animal without untoward results, and in all his experiments he never noted a rise in pressure after such injections.

This detoxification of iodine he showed was due to a chemical combination of iodine with the proteids of the blood. I accordingly suspected that just as elementary iodine combined with proteids, so it was possible that iodine in ionic state, such as we have in our substituted Locke solutions, might also combine with the blood plasma and thus lose its physiological properties.

To test this, mixtures were made of normal pig's serum with various Locke solutions, and the pharmacological action of such mixtures studied on heart and blood vessels.

It was found that the action of potassium or sodium ions is not at all inhibited by the blood serum, the effect of iodine ions however may be completely obliterated. Thus a Locke solution in which the NaCl was wholly substituted by its equimolecular weight of NaI, is a powerful vaso-constrictor and cardiac stimulant. If, however, such a solution be mixed with two parts of serum, the effect of iodine is entirely inhibited, and the action on heart and vessels is the same as that obtained with normal Locke solution and serum mixed in the same proportions (Fig. 8A). The *iodine* ions have combined with the plasma. A larger proportion of iodine ions mixed with serum leaves some

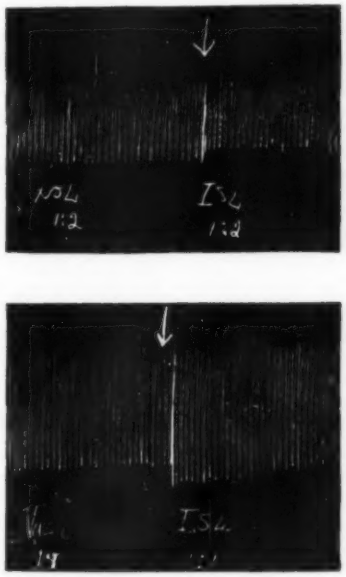

Fig. 8.—Frog's heart; suspension method. Systole = down-stroke.

A.—Normal Locke, plus normal serum 1:2, and iodine Locke, plus normal serum 1:2.

B.—Normal Locke, plus normal serum 1:1; normal Locke, plus normal serum 1:1.

of the iodine uncombined and hence produces a slight stimulation (Fig. 8B).

Discussion and Summary.

From the above experiments it will be seen that the potassium ion produces a relaxation of the blood vessels and a marked depression of the heart; that the sodium ion has a slightly stimulating action on the blood vessels and also stimulates the heart, and that the iodine ion is a powerful stimulant to both the heart and blood vessels as shown by its action in experiments on isolated organs. The stimulating effect of the iodine ions, however, is greatly inhibited in the intact animal by their chemical combination with the proteids of the blood.

Whether the chemical compound thus produced is a stable one, or whether it is a loose one, and slowly breaks up, setting iodine free, remains an open question. If iodine is set free, a stimulating effect is to be expected.

The action of sodium and potassium iodides on the heart and vessels can be best understood from the action of their component factors. Sodium iodide possesses no depressing property, for the sodium ion is a vascular constrictor and a cardiac stimulant, and the iodine ion, in so far as it is free to act, has the same action.

Potassium iodide, on the other hand, clearly shows the depressing effect of the potassium ion on the heart and vessels, especially of mammals, not only on isolated organs, but also in the living animals. It is therefore not a matter of indifference which of the iodides is to be chosen for the purpose of depressing the circulation, as, for instance, in case of an aneurism. The above pharmacological analysis of the action of the iodides, furthermore, shows that so far as experimental evidence goes, the iodides possess no special virtue of lowering blood pressure, but that that effect is really due entirely to the potassium, and could be produced even more efficiently by other potassium salts.

Addendum: After this paper went to press, two publications appeared which are interesting to note in this connection. A. Lehndorff in the Arch. f. Exp. Path. u. Ther., Vol. 76, p. 224, calls attention to the stimulating action of iodine on the blood-vessels; and J. Schwalbe in the Deut. Med. Wochenschrift, Nos. 14 and 15, 1914, summarizes the opinions of the most prominent German clinicians on the use of iodides in arteriosclerosis, the weight of opinion being unfavorable to the drug.

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NOTES ON NEW BOOKS.

A Text-Book of Medical Entomology. By Walter Scott Patton, M. B., etc., and Francis William Cragg, M. D., etc. £1-1-0. (*London, Madras and Calcutta: Christian Literature Society for India, 1913.*)

This volume is the outgrowth of the rich experience of these authors at the King Institute at Madras, India. By a fortunate arrangement of material, it will serve, not only as an advanced text-book, but also as a valuable reference work.

In considering the relationship between insects and disease, proportionally more space has been given to the entomological features than to the medical aspects of the subject. A very comprehensive description is given of the blood-sucking arthropods, not only of India, but throughout the world. The types described are not restricted to those of recognized importance on the liberal basis that "a certain breadth of view is essential to progress." Especial attention is given to Williston's North American Diptera and to the work of Banks and Stiles on American Ticks.

In the section on practical laboratory methods, careful attention is given to the methods of rearing and infecting insects and to the anatomical examination for evidences of infection. From their wide experience in this subject the authors are able to give extremely helpful details which, though they are of a minor nature, are often so essential to success.

This volume is of especial interest to the investigator. It abounds in original material. Numerous pitfalls of experimental work are pointed out and a careful consideration is given to the methods of avoiding confusion between the natural protozoan fauna of insects and pathogenic parasites.

To the person approaching the subject from purely the medical standpoint, it might be possible to make the subject matter a little more accessible. For instance, it seems a little unexpected not to find such diseases as malaria, bubonic plague, or dengue, mentioned in the index, though omissions in an index of the first edition of a work should perhaps not be mentioned.

The volume is profusely illustrated with clear black and white drawings. In all there are probably more than 500 figures. To the medical man it might add a little interest to represent lesions in insects produced by parasites such as the organisms of malaria or representations of the stage of the life cycle of the parasites during their development in the invertebrate host.

The authors have condensed an immense amount of accurate information into a very convenient form. It is the most comprehensive work on this subject and has a very wide field for its application.

An Introduction to the History of Medicine. With medical chronology, bibliographic data and test questions. By Fielding H. Garrison, A. B., M. D., Principal Assistant Librarian, Surgeon-General's Office, Washington, D. C. Illustrated. 763 pp. 8°. (*Philadelphia and London: W. B. Saunders Company, 1913 (1914).*)

This book marks an epoch in American medical literature. Not only does it register the contributions of a newer civilization in their proper historical relation to those of the world at large, but in it for the first time an American writer, in fulfillment of an evident want, offers a comprehensive treatise of a universal history of medicine.

This book, fitly dedicated to the librarian of the Surgeon-General's Office, Colonel Walter D. McCaw, does not pretend to be more than an introduction into the vast fields of medical history. The author wishes, as he says himself, to act only as an interpreter of "the best that has been thought and said," and not to attempt a learned or lengthy exposition. It may be stated right here that his book fulfills his aim admirably and that it offers even more than its modest title indicates. The clearness, conciseness and perspicacity of its statements, the accuracy of its references alone will insure a permanent value to this book. A detailed analysis is obviously impossible, for although intended only as an introduction, the amount of material brought together is stupendous. It treats effectively the various aspects of medical endeavor from earliest times to our own days, a range which more pretentious books have not been able to cover. One would presume *à priori* that such a guide through the immense records of the past within a limited space must be of necessity a dry-as-dust enumeration of persons, discoveries and other prominent features. By a very happy combination of talents, those of the historian, physician and narrator, the author has been able to elude this presumption successfully. Wherever one opens the book one is captivated at once by the easily flowing narrative which takes one *in medias res* without unnecessary preamble. The men of mark stand out in bold relief, often visualized by superb portraits, which evidence most careful selection. The characteristics of a given period with its fitful changes of method, the fall and rise of opinions and doctrines, their intrinsic importance and proper correlation to cultural conditions are handled with fine circumspection. No profound psychologic or philosophic analysis is attempted and still the matter is presented in a way which stimulates thinking, comparison and further study. With rapid, telling strokes the main features are given, and, as a sketch from a skillful brush often presents by that greater art of judicious elimination a more striking likeness to reality than the finished picture, so the perusal of this book leaves in the reader's mind more distinct and easily remembered impressions than the more elaborate exposition in greater works. Especially successful is the biographical treatment of the various pathfinders and epochmakers in medical history. The sketches of Harvey, Boerhaave, Haller, Pasteur, Virchow and others, though by no means only echoing traditional opinions, are little masterpieces to which casual anecdotes lend a peculiar charm and color. The finely thoughtout chapter on the identity of all forms of ancient and primitive medicine, the introduction to the one on Greek medicine, the one on the 17th century as the age of individual scientific endeavor, on the beginning of organized advancement of science in the 19th and of organized preventive medicine in our century, offer much thought and inspiration, even to those who will perhaps differ in the just assignment of values. No one, not even the most "practically" inclined practitioner, if he reads at all, can lay the book aside without feeling lifted above the drudgery of daily routine, without a warmer interest in the aims of his art and science; and, perhaps somewhat humbled in his overestimation of current advances, he will become conscious of that almost intangible bond of human kinship between those of all times who have made the relief of pain and disease their task.

As regards the form, the technical construction of the book, it evinces everywhere that methodical procedure which so notably distinguishes the bibliographic productions of the great national institution in Washington. Ample and accurate references, chronological tables, subject and author indices, suggestions for collateral reading are provided and offer, without disturbance to the casual reader, most valuable assistance to the student and to those desiring a ready reference book on historical questions. Certain errors and omissions in a work like this are unavoidable; one can only wonder that there are so few considering the bewildering mass of data, names and facts which had to be sifted.

Other editions of this book, and many we hope may be called for, will efface such slips, which hardly affect the great usefulness of the work as it stands. I cannot refrain, in conclusion, from noting that the book has already received a warm commendation from Prof. Karl Sudhoff. No other review can offer a greater encouragement to the author than this unstinted praise from the acknowledged leader in scientific historical research. It is to be hoped that Sudhoff is right when he thinks that in English-speaking countries the book will do more good and make more converts for historical thinking than the greater standard works.

A few misprints have been noted:

P. 301, 20 lines from top, for 1162 read 1762.
P. 307, 7 lines from top, for University of Virginia read Williamsburg, Va.
P. 637, 5 lines from top, for Annemese read Annemasse.
P. 649, 2 lines from bottom, for 1890 read 1876.

A. C. K.

International Clinics. Vol. I. 24th Series. Edited by HENRY W. CATTELL, M. D., and associates. $2. (*Philadelphia and London: J. B. Lippincott Company, 1914.*)

This volume opens with two noteworthy papers by Philadelphia physicians, the first by Willson on "The Treatment of Nephritis," and the second by Taylor on "Cardiovascular-renal Regulation by other Means than Drugs," and closes with an interesting review of the "Progress of Medicine" during 1913. Between these are interspersed other papers to appeal to specialists in various branches of medicine and surgery.

Diseases of the Heart. By JAMES MACKENZIE, M. D., F. R. C. P., etc. Third Edition. (*London: Henry Frowde and Hodder & Stoughton, 1913.*)

I note with pleasure the appearance of the third edition of this interesting and stimulating book by the great pioneer in the field of modern cardiac and vascular diseases. Though the body of the work is not much altered, much more use is made of the knowledge gained by means of the electrocardiograph than in the previous editions. The book is considererably enlarged and enriched from the tremendous store of clinical cases studied with an unparalleled thoroughness and precision under Dr. Mackenzie's personal observation and is fuller than ever of excellent suggestions for clinical practice. It is a compilation of the original views and practices of Dr. Mackenzie and is in no sense a systematic text book to present the entire field of cardiac diseases. The reader should not approach the book with this expectation.

Especially noteworthy is the emphasis that Mackenzie lays upon the fact that digitalis is ineffective where the heart muscle has suffered from bacterial or other intoxications, which is often realized more in theory than in practice. The chapter upon the use of digitalis in auricular fibrillation is especially interesting.

The brilliant style of the author and the excellent typographical work of the publishers, which added much to the previous editions, are pleasing features of this one as well. A. D. H.

Progressive Medicine. Edited by HOBART AMORY HARE, M. D., etc. Vol. I. (*Philadelphia and New York: Lea & Febiger, March, 1914.*)

This volume is shared by surgery, medicine, diseases of children, rhinology, laryngology and otology; and in each chapter the compilers present clearly and concisely the latest views as held by the leading specialists on many diseases and conditions. The résumés are well done and are intended to serve merely as guides for busy practitioners who may not be able to use the original sources, or who have too large a clientèle to find time for exhaustive reading.

THE QUARTER CENTENNIAL ANNIVERSARY OF THE OPENING OF THE JOHNS HOPKINS HOSPITAL AND THE TWENTY-FIRST ANNIVERSARY OF THE OPENING OF THE MEDICAL SCHOOL

Will be observed by appropriate exercises beginning October 5, 1914, and continuing during the week.

The exercises upon Monday, October 5, 9.30 a. m. to 12 m., are to be especially arranged for by the Training School for Nurses and will be announced later.

Upon Monday at 3.30 p. m., the formal opening meeting will be held at the Lyric, with addresses by Dr. W. H. Welch, Sir William Osler, Miss M. Adelaide Nutting and Dr. H. M. Hurd.

In the evening there will be dinners of the former Medical Officers of the Hospital, and of the Alumnæ of the Training School for Nurses.

Upon Tuesday, October 6, 9.30 a. m. until 12 m., papers upon medicine by former members of the staff will be presented in the Medical Amphitheatre. Papers or demonstrations of methods of study of Psychiatry at the Henry Phipps' Clinic from 10 a. m. to 12 m. Gynecological operations in the Surgical Amphitheatre from 10 a. m. until 1 p. m. A Clinic by Sir William Osler at 12 m.

Luncheon at the Hospital from 1 to 2.30 p. m.

From 2.30 to 3.30 p. m. Clinic in the Harriet Lane Home by Dr. John Howland. At 3.30 p. m., a dedication of the Hewetson Medallion.

A demonstration of Nurses' work in the Medical Amphitheatre from 4 to 5 p. m.

From 4.30 to 5.30 p. m., a lecture on the Herter Foundation by Dr. Thomas Lewis of London.

In the evening a Dinner of the Alumni of the Medical School.

Wednesday, October 7, from 9.30 a. m. to 1 p. m., Surgical Operations in the Surgical Amphitheatre.

From 11 a. m. to 1 p. m. Visits to Medical Laboratories.

1 p. m., Luncheon.

At 3.30 p. m., Dedication of the James Buchanan Brady Urological Clinic, with addresses by Dr. Winford Smith, President Goodnow of The Johns Hopkins University, Dr. H. H. Young, and others.

A Garden Party upon the lawn of the Hospital at 5 p. m.

In the evening a Subscription Dinner to Mr. James Buchanan Brady. Also Class Dinners.

Thursday, October 8, 9.30 a. m. to 1 p. m., Papers in Pathology in the Medical Amphitheatre.

Also Papers or Addresses upon Obstetrical Topics in the Surgical Lecture Room, 10 a. m. to 12 m. Operations in Urological Surgery in the Surgical Amphitheatre, 10 a. m. to 12 m.

1 to 2.30 p. m., Luncheon.

4.30 p. m., Second Herter Lecture by Dr. Lewis.

In the Evening, Class Dinners.

Friday, October 9, 4.30 p. m., Third Herter Lecture by Dr. Lewis.

More detailed programmes will be published later.

During the Anniversary Week laboratory demonstrations will be given in the laboratories of the Medical School as follows:

In the Anatomical Laboratory, By Prof. Mall and the Anatomical Staff.

In the Physiological Laboratory, By Prof. Howell and the Physiological Staff.

In the Pharmacological Laboratory, By Prof. Abell and the Pharmacological Staff.

The exact dates and hours of such demonstrations will be announced in the final program.

PROGRAMME FOR THE CELEBRATION OF THE TWENTY-FIFTH ANNIVERSARY OF THE OPENING OF THE JOHNS HOPKINS HOSPITAL

MONDAY October 5	TUESDAY October 6	WEDNESDAY October 7	THURSDAY October 8
9.30–12 Nurses' Training School	9.30–12 Medicine (Medical Amphitheatre) Psychiatry 10–1 Gynecology (Surgical Amphitheatre) 12 Clinic Sir William Osler	9.30–1 Surgery (Surgical Amphitheatre) 11–1 Medical Laboratories	Pathology (Medical Amphitheatre) Obstetrics (Surgical Lecture Room) 10–12 Urological Surgery (Surgical Amphitheatre)
	1–2.30 Luncheon	Luncheon	Luncheon
3.30 Opening Meeting (The Lyric) Addresses: Dr. W. H. Welch presiding Sir Wm. Osler Dr. H. M. Hurd Miss M. A. Nutting	2.30 Pediatric Wards Dr. Howland 3.30 Dedication Hewetson Medallion 4.30 Herter Lecture	3.30 Dedication of the J. B. Brady Urological Clinic Dr. W. H. Smith presiding Pres. F. J. Goodnow Dr. H. H. Young and other speakers 5 Garden Party (The Lawn)	4.30 Herter Lecture
Dinners Johns Hopkins Hospital Alumni Nurses	Dinner Alumni of Medical School	Dinner to Mr. J. B. Brady, Donor of the new Urological Clinic Class Dinners	Class Dinners

THE HERTER LECTURES FOR 1914.

The Herter Lectures will be given in connection with the Quarter Centennial Anniversary of the Opening of The Johns Hospital and the Twenty-first Anniversary of the Opening of the Medical Department of The Johns Hopkins University, upon Tuesday, Thursday and Friday, October 6, 8 and 9, 1914, at the Physiological Lecture Room, Monument and Washington Streets, at 4.30 p. m., by Thomas Lewis, M. D., University College, London, England.

Dr. Thomas Lewis in charge of the heart station at University College, and Editor of *Heart* has done important work in the study of cardiac conditions, and will present three lectures on the scientific study of the heart and its bearing on clinical medicine. He is the first clinical investigator who has filled the position of Herter Lecturer. The titles of his lectures will be announced later.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Subscriptions, $2.00 a year (foreign postage, 50 cents), may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each. Single copies may also be procured from the BALTIMORE NEWS CO., Baltimore.